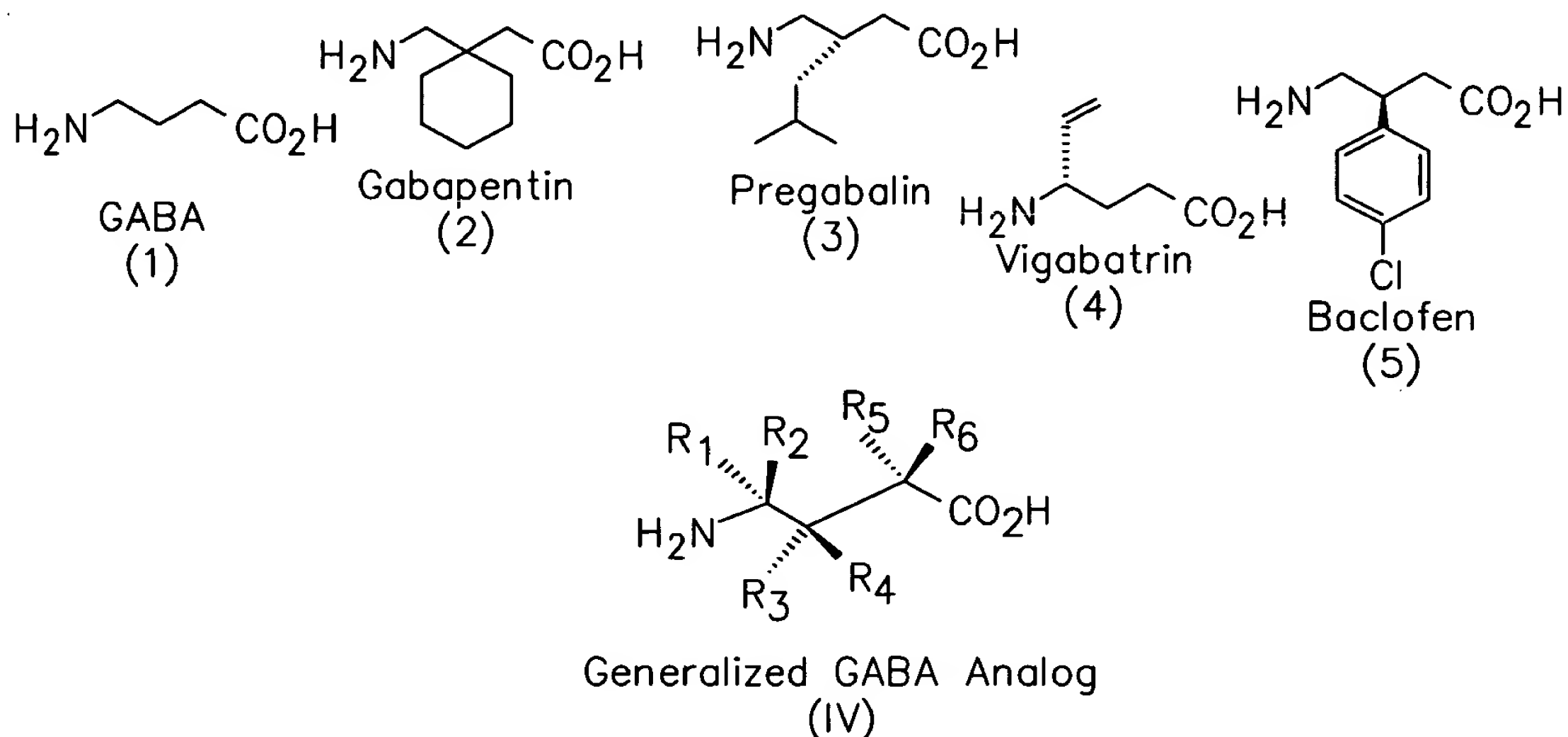


#3

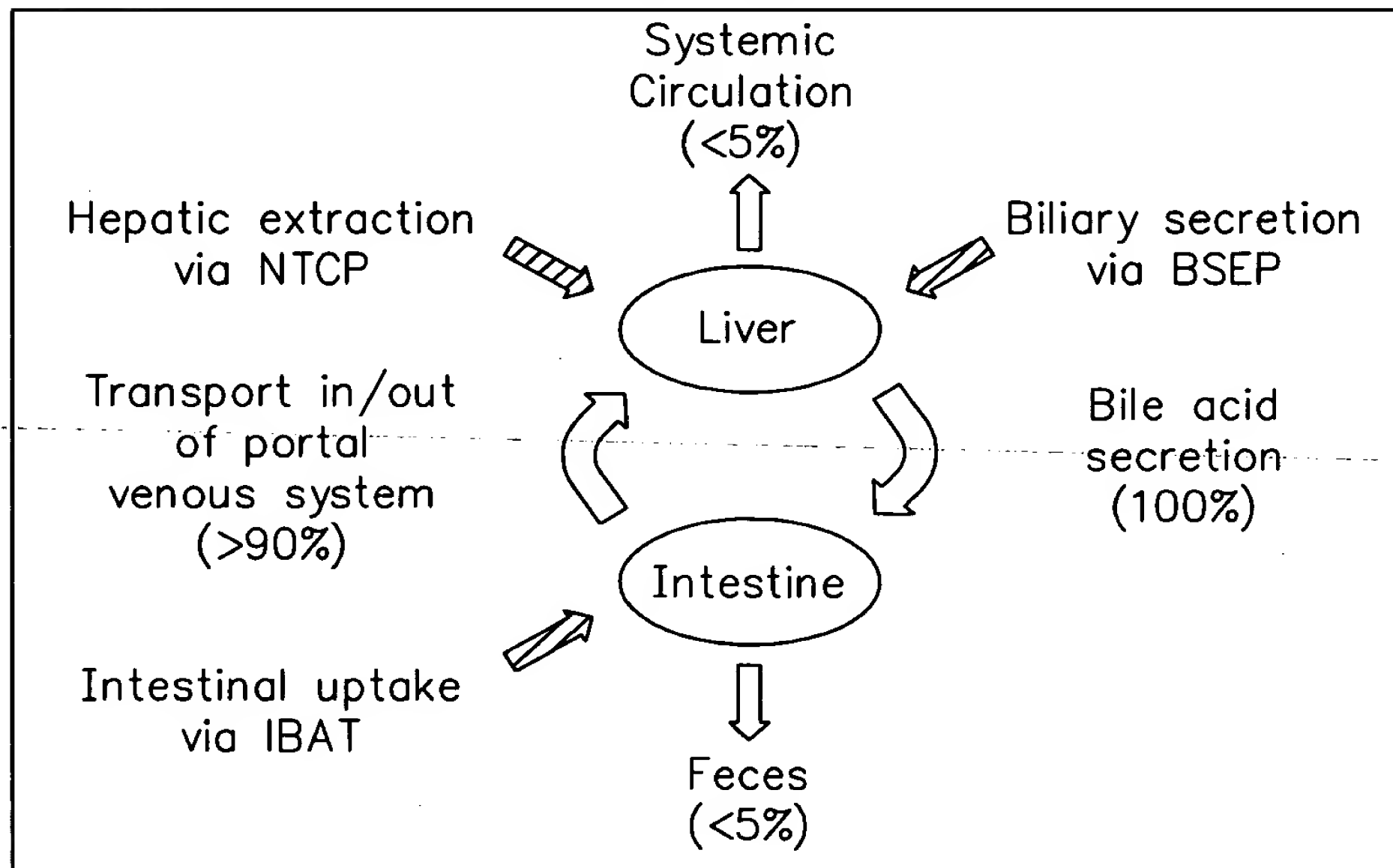
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**FIG. 1**



**FIG. 2**

*The Enterohepatic Circulation with Key Transporter Proteins Mediating Bile Acid Circulation*

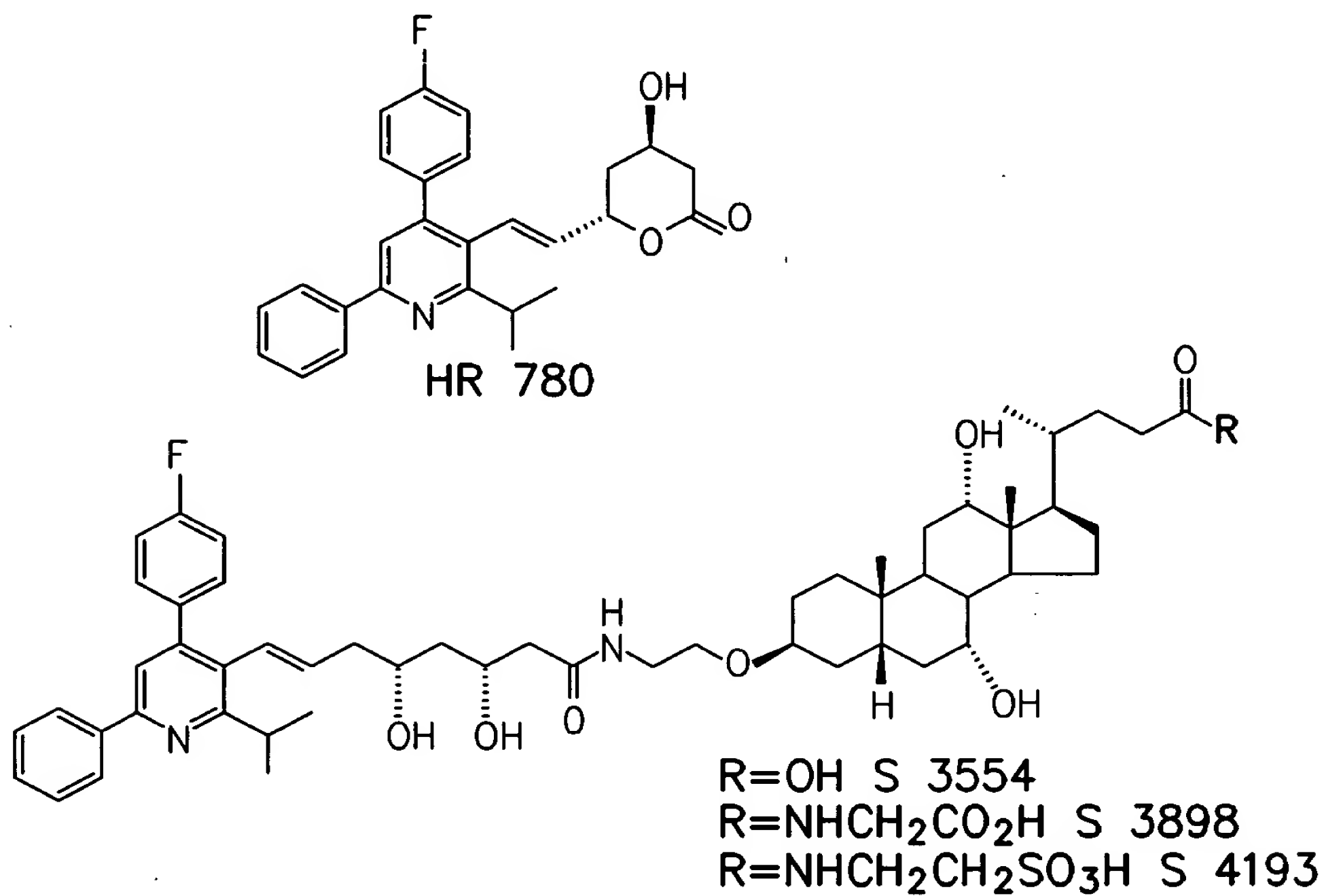


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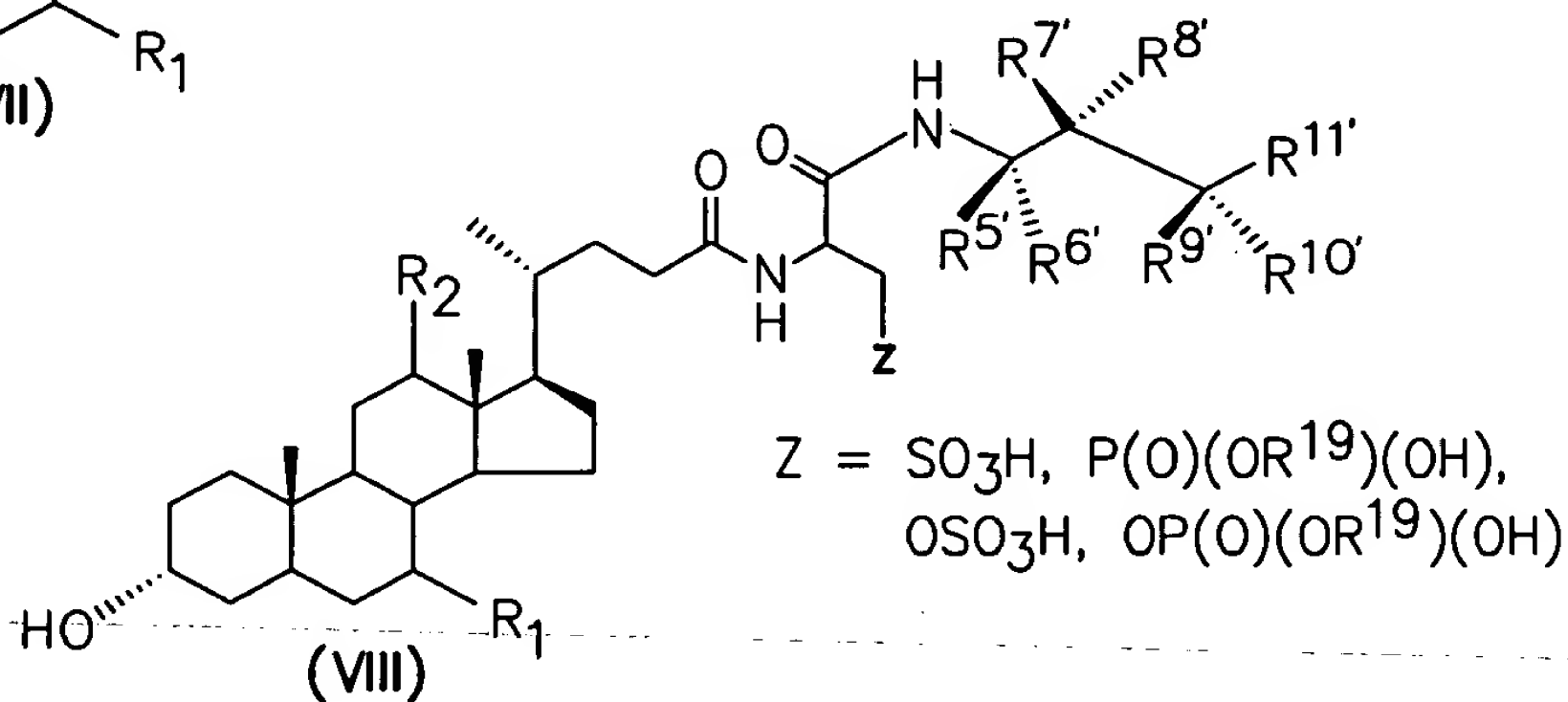
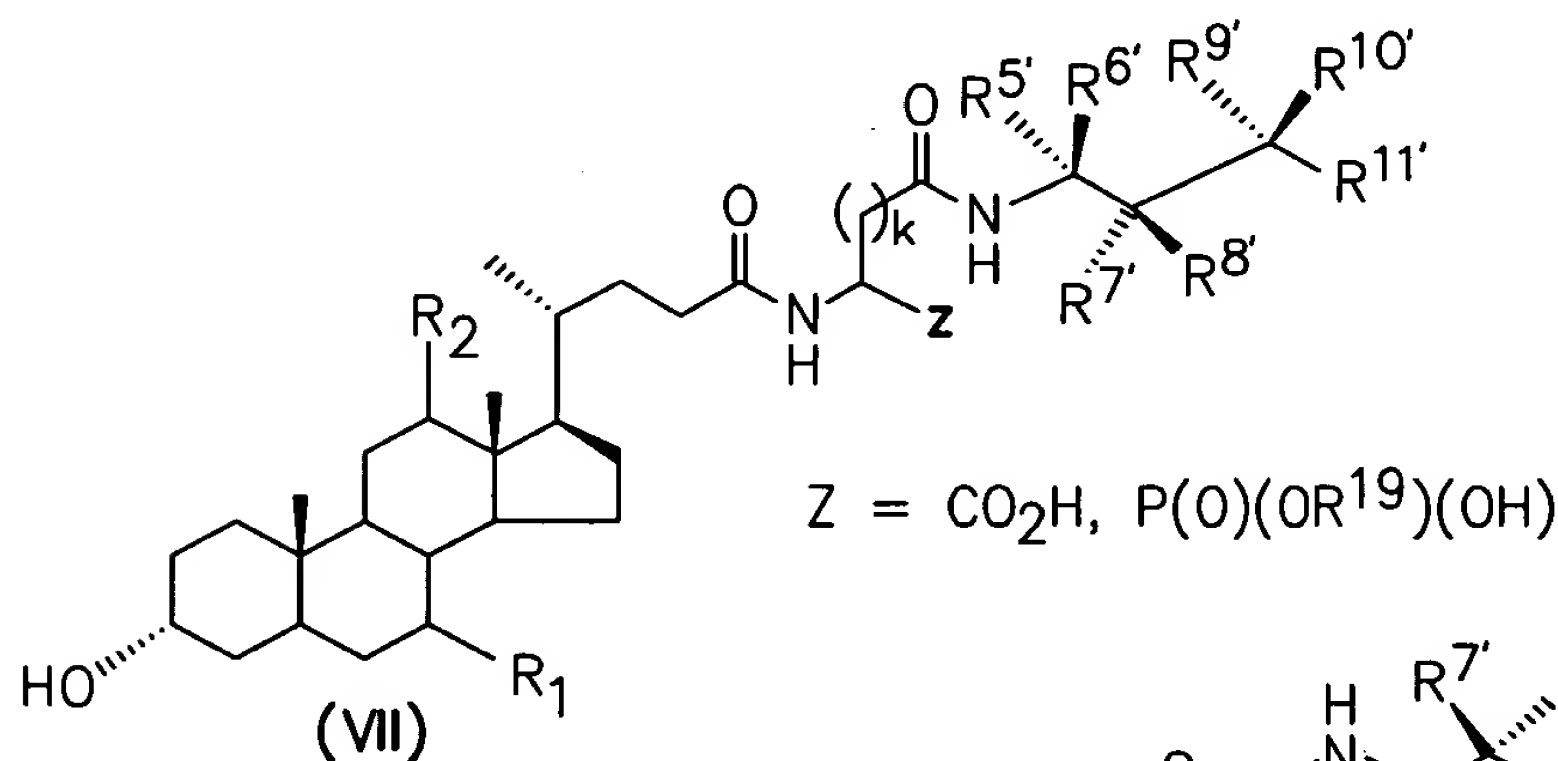
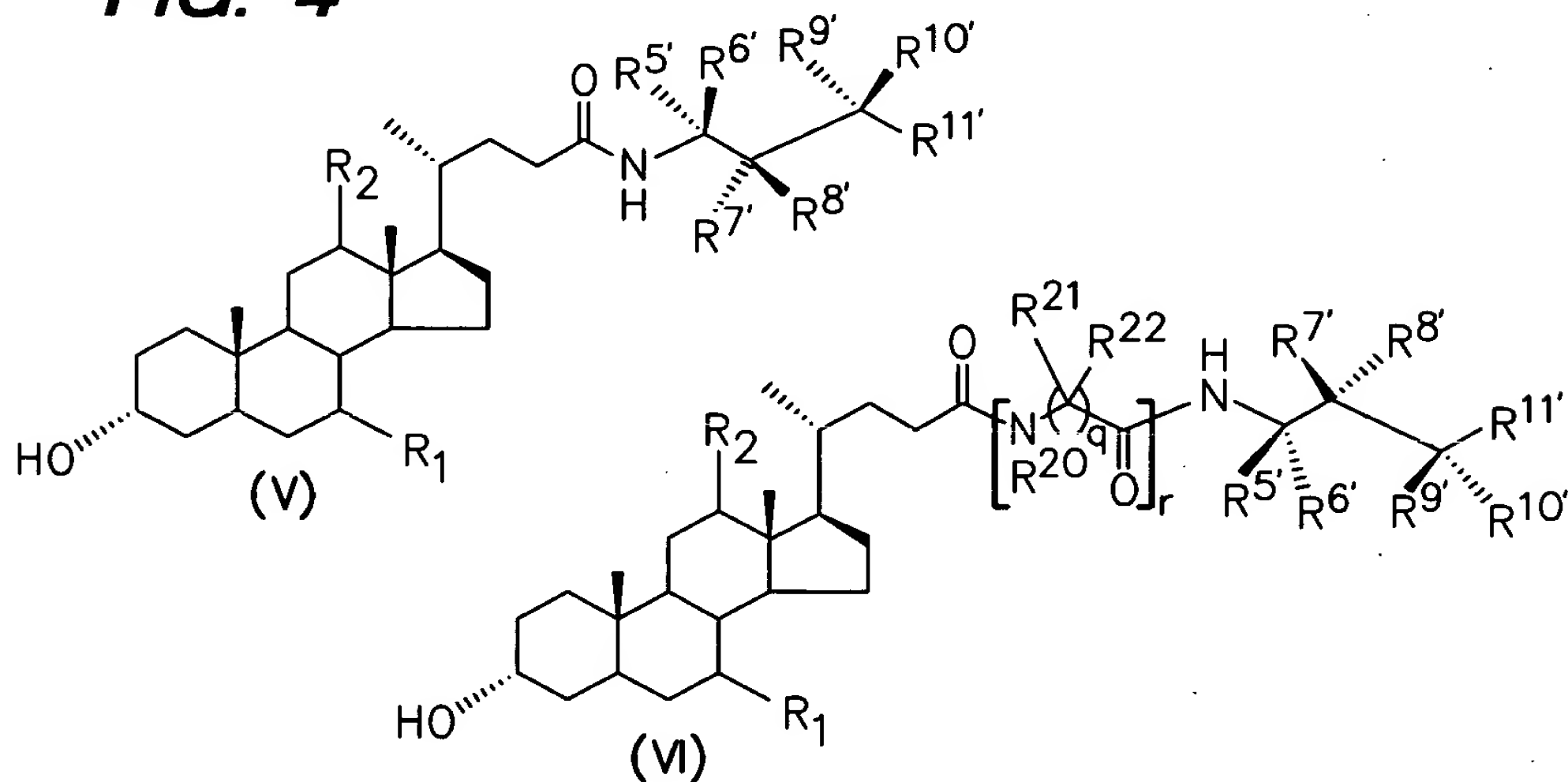
**FIG. 3**

*Bile Acid Conjugates of HMG-CoA Reductase Inhibitor*



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**FIG. 4** 3/31

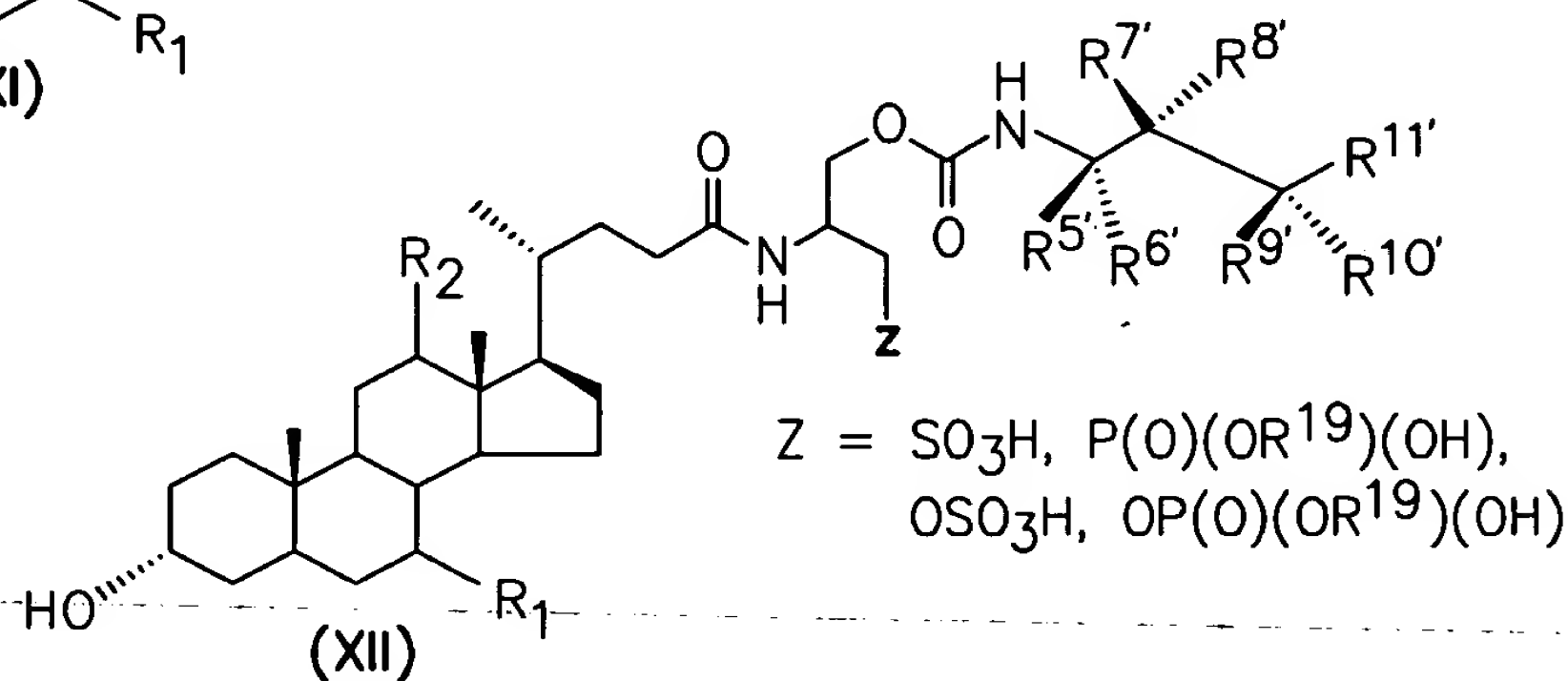
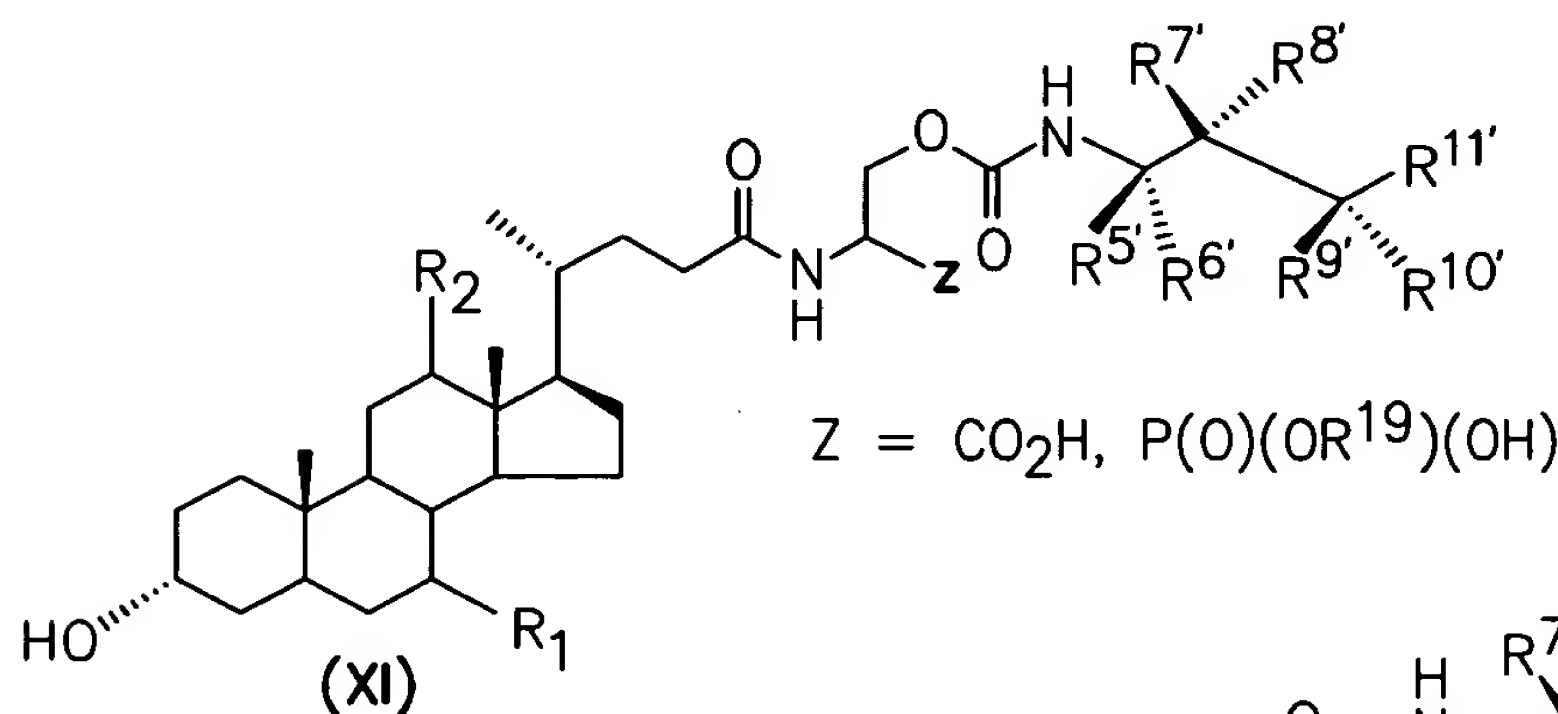
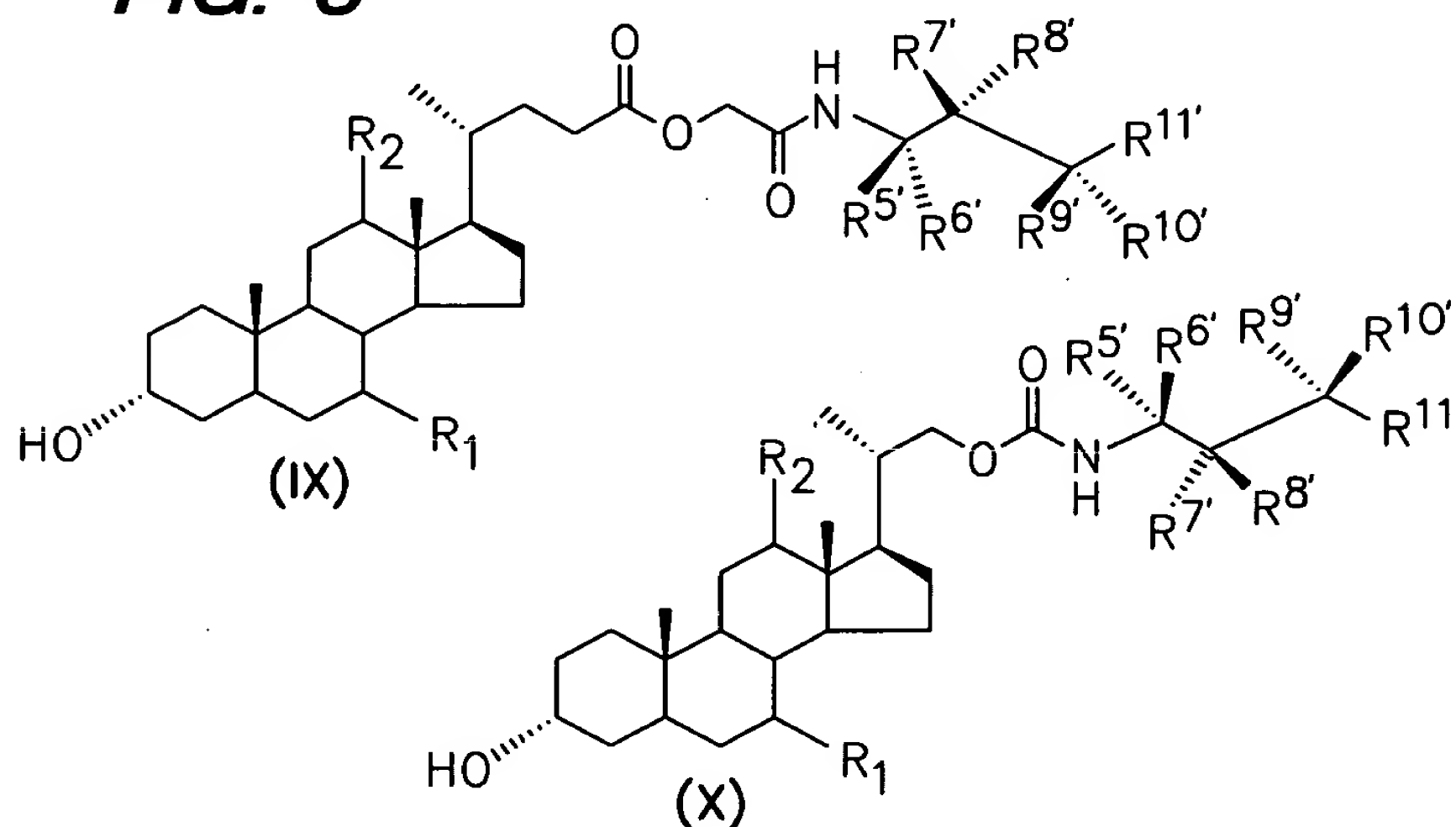


R<sub>1</sub> = α-OH; R<sub>2</sub> = α-OH (Cholate)  
 R<sub>1</sub> = β-OH; R<sub>2</sub> = H (Ursodeoxycholate)  
 R<sub>1</sub> = α-OH; R<sub>2</sub> = H (Chenodeoxycholate)  
 R<sub>1</sub> = H; R<sub>2</sub> = α-OH (Deoxycholate)  
 R<sub>1</sub> = β-OH; R<sub>2</sub> = α-OH (Ursocholate)  
 R<sub>1</sub> = H; R<sub>2</sub> = H (Lithocholate)

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**FIG. 5**

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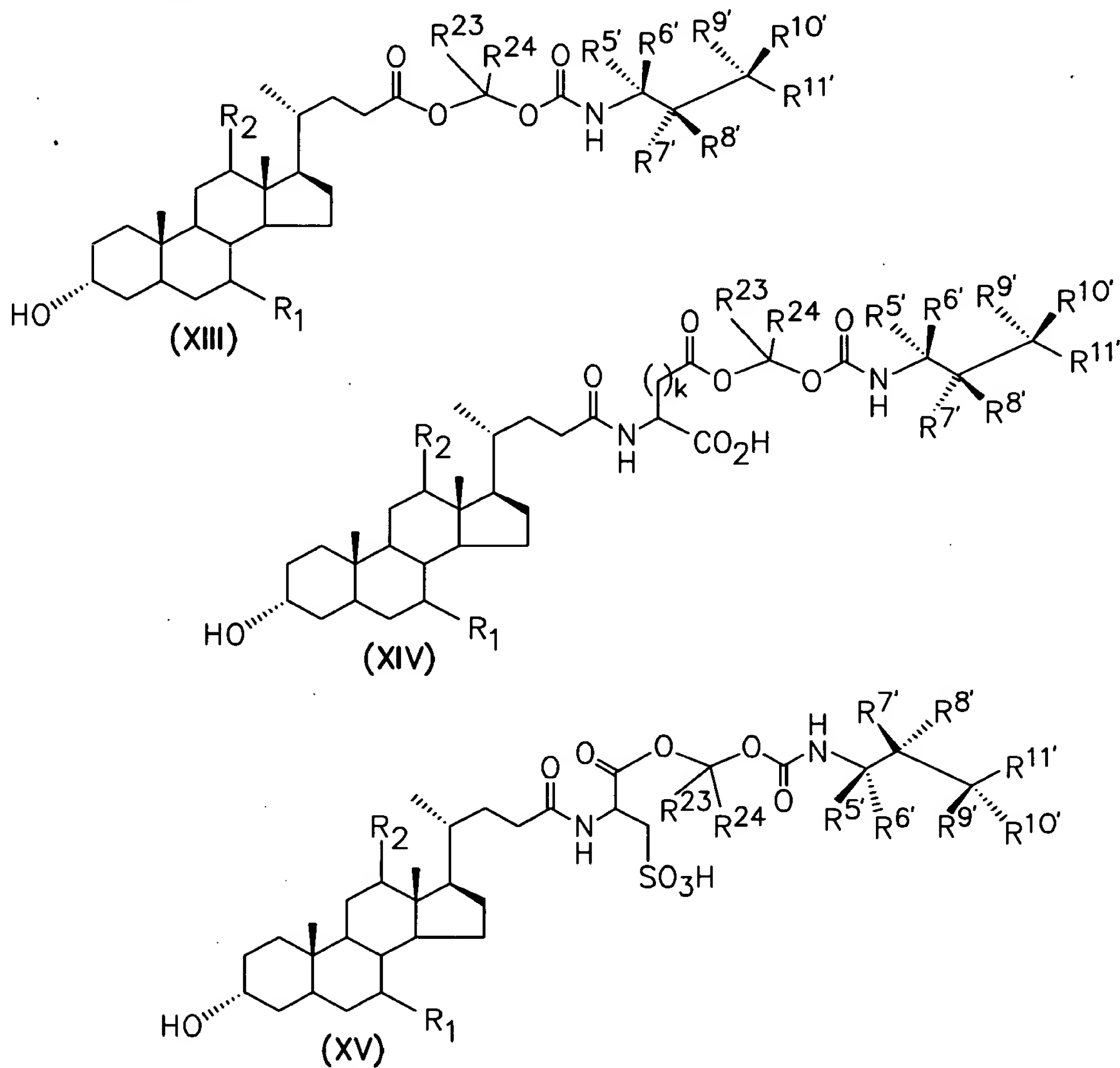


- R<sub>1</sub> = α-OH; R<sub>2</sub> = α-OH (Cholate)
- R<sub>1</sub> = β-OH; R<sub>2</sub> = H (Ursodeoxycholate)
- R<sub>1</sub> = α-OH; R<sub>2</sub> = H (Chenodeoxycholate)
- R<sub>1</sub> = H; R<sub>2</sub> = α-OH (Deoxycholate)
- R<sub>1</sub> = β-OH; R<sub>2</sub> = α-OH (Ursocholate)
- R<sub>1</sub> = H; R<sub>2</sub> = H (Lithocholate)

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FIG. 6

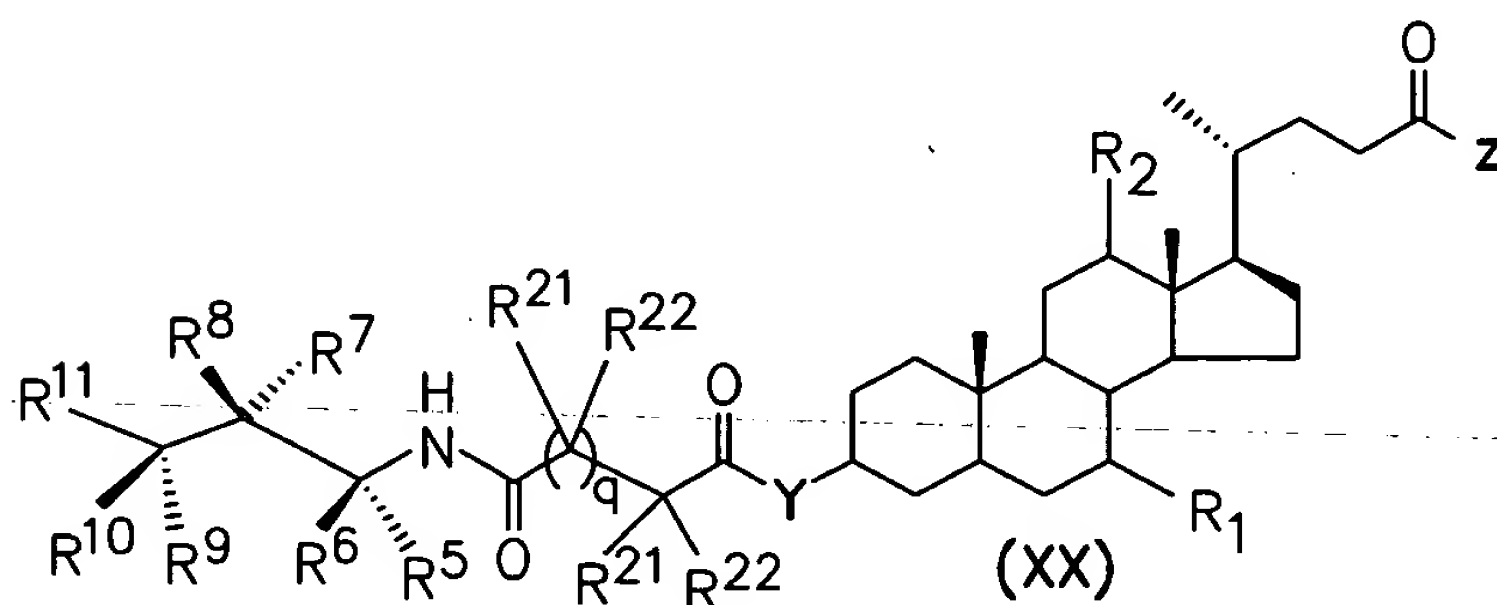
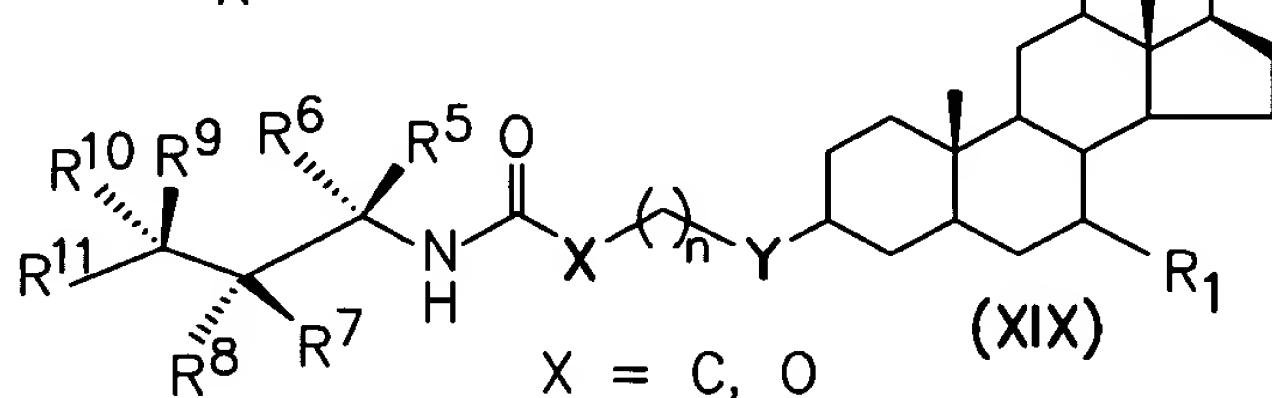
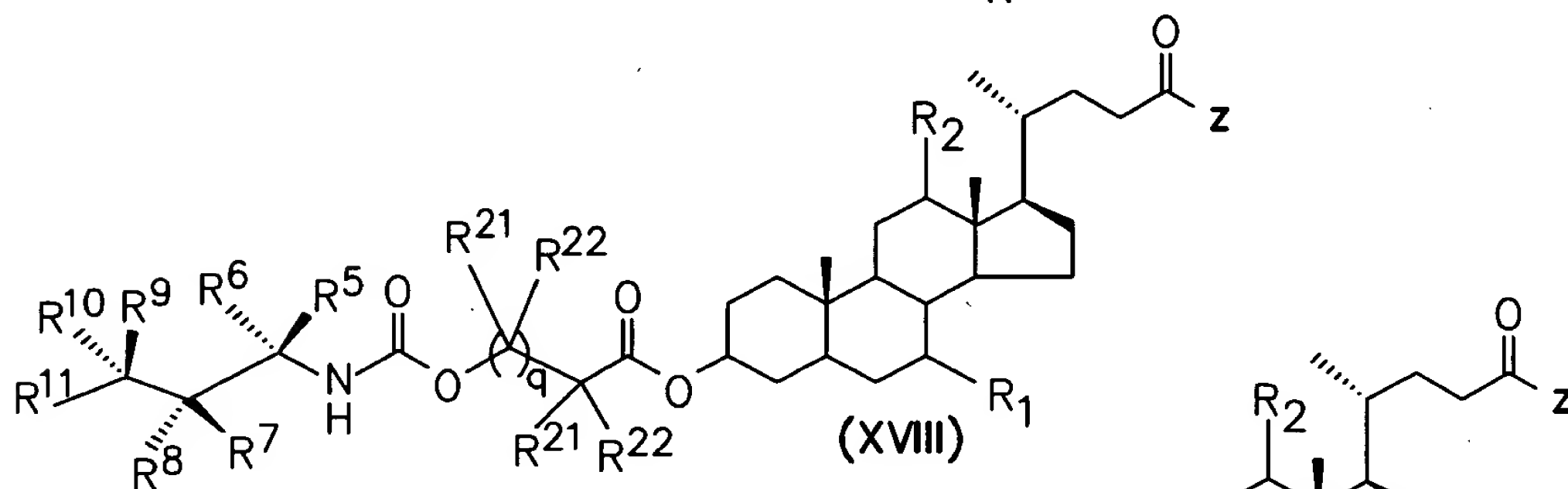
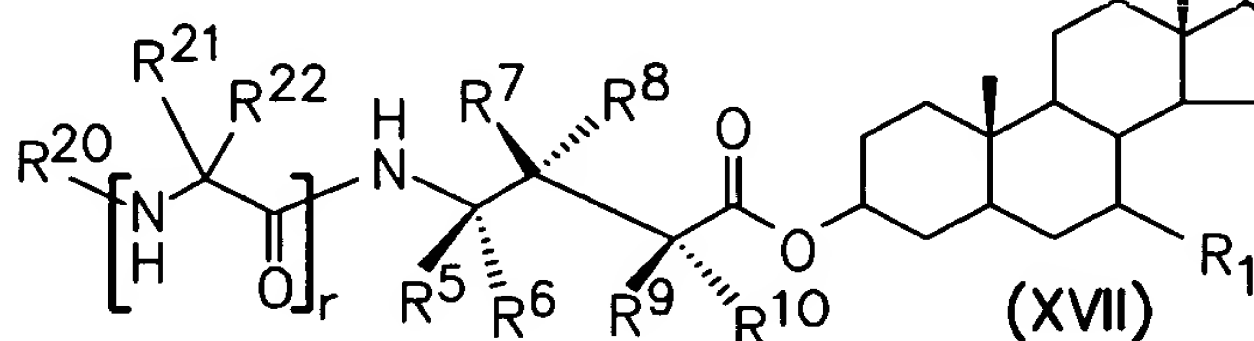
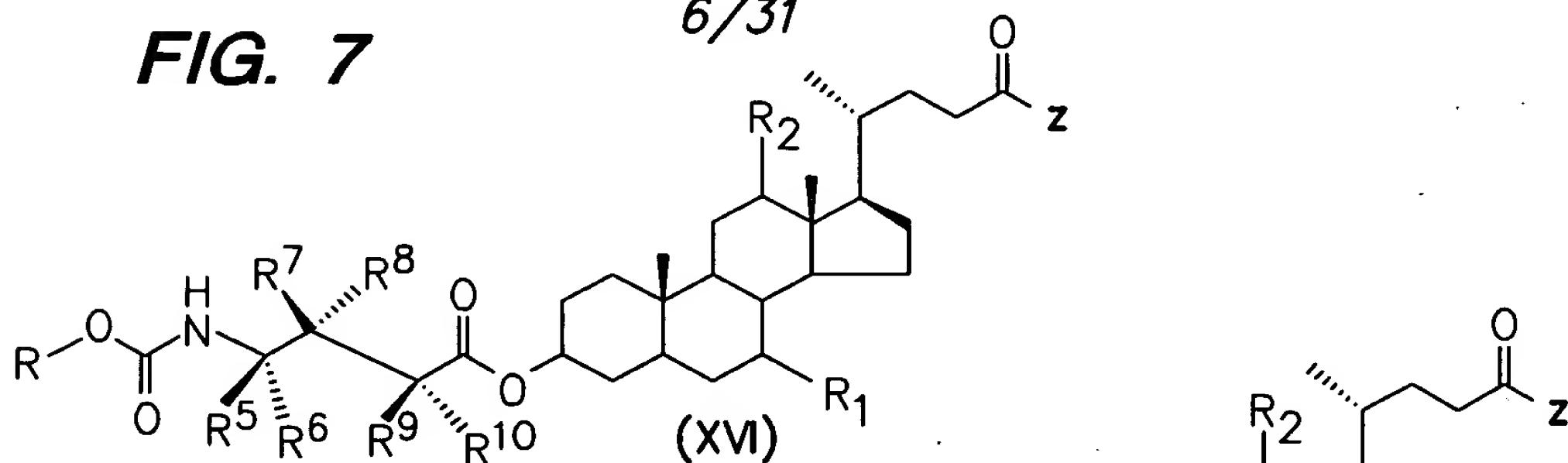


R<sub>1</sub> = α-OH; R<sub>2</sub> = α-OH (Cholate)  
 R<sub>1</sub> = β-OH; R<sub>2</sub> = H (Ursodeoxycholate)  
 R<sub>1</sub> = α-OH; R<sub>2</sub> = H (Chenodeoxycholate)  
 R<sub>1</sub> = H; R<sub>2</sub> = α-OH (Deoxycholate)  
 R<sub>1</sub> = β-OH; R<sub>2</sub> = α-OH (Ursocholate)  
 R<sub>1</sub> = H; R<sub>2</sub> = H (Lithocholate)

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**FIG. 7**

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R1 =  $\alpha$ -OH; R2 =  $\alpha$ -OH (Cholate)  
 R1 =  $\beta$ -OH; R2 = H (Ursodeoxycholate)  
 R1 =  $\alpha$ -OH; R2 = H (Chenodeoxycholate)  
 R1 = H; R2 =  $\alpha$ -OH (Deoxycholate)  
 R1 =  $\beta$ -OH; R2 =  $\alpha$ -OH (Ursocholate)  
 R1 = H; R2 = H (Lithocholate)

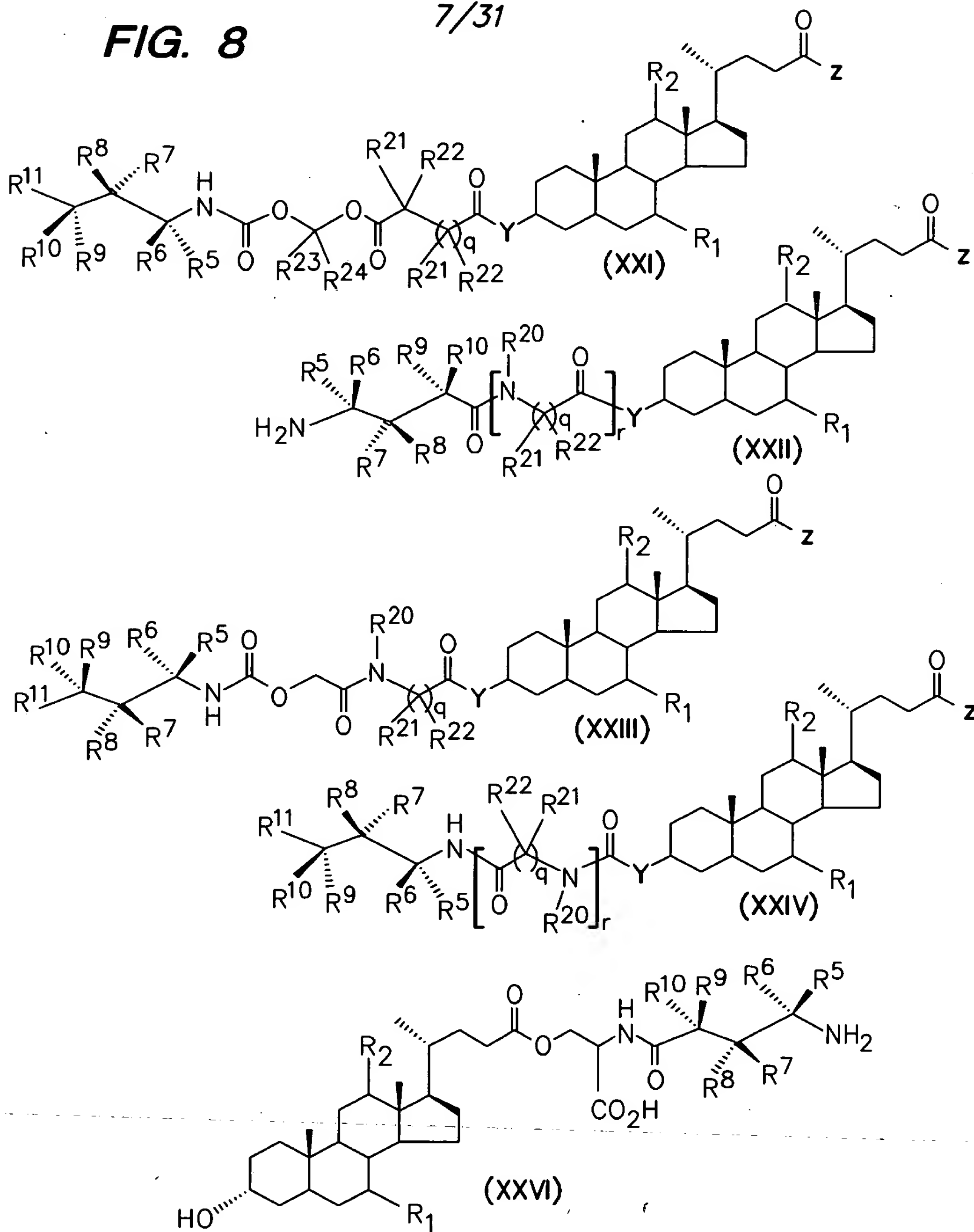
Y =  $\alpha$ -O  
 Y =  $\beta$ -O  
 Y =  $\alpha$ -NH  
 Y =  $\beta$ -NH

Z = OH  
 Z =  $\text{N}(\text{H})\text{CH}_2\text{CO}_2\text{H}$   
 Z =  $\text{N}(\text{H})\text{CH}_2\text{SO}_3\text{H}$

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**FIG. 8**

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R1 =  $\alpha$ -OH; R2 =  $\alpha$ -OH (Cholate)  
 R1 =  $\beta$ -OH; R2 = H (Ursodeoxycholate)  
 R1 =  $\alpha$ -OH; R2 = H (Chenodeoxycholate)  
 R1 = H; R2 =  $\alpha$ -OH (Deoxycholate)  
 R1 =  $\beta$ -OH; R2 =  $\alpha$ -OH (Ursocholate)  
 R1 = H; R2 = H (Lithocholate)

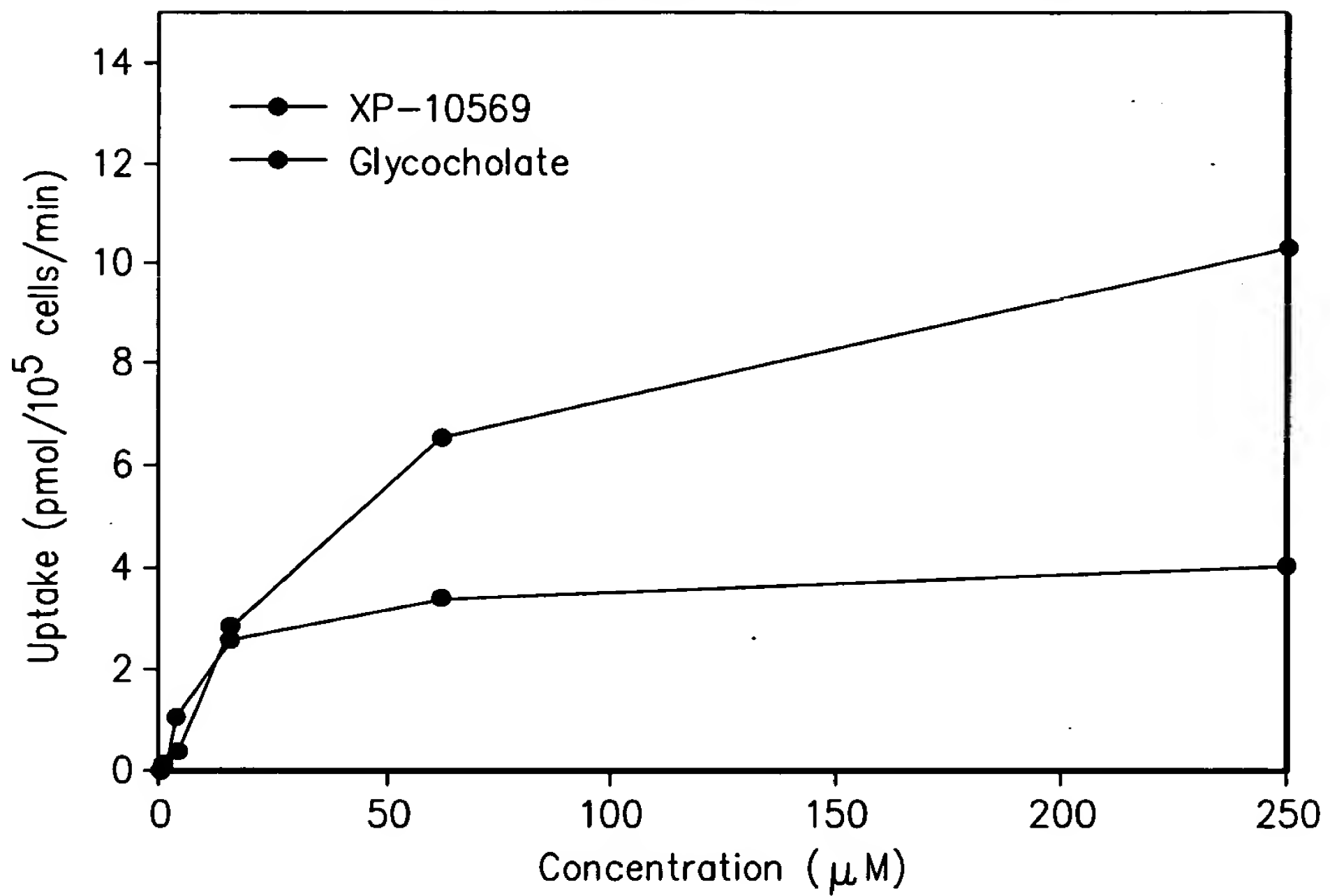
Y =  $\alpha$ -O  
 Y =  $\beta$ -O  
 Y =  $\alpha$ -NH  
 Y =  $\beta$ -NH

Z = OH  
 Z =  $\text{N} \begin{array}{c} \text{H} \end{array} \text{CH}_2 \text{CO}_2\text{H}$   
 Z =  $\text{N} \begin{array}{c} \text{H} \end{array} \text{CH}_2 \text{SO}_3\text{H}$

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**FIG. 9** Uptake of (8) (XP10569) or Glycochocholate by IBAT-Transfected CHO Cells



**FIG. 10** Uptake of (8) (XP10569) or Glycocholate by LBAT-Transfected CHO Cells

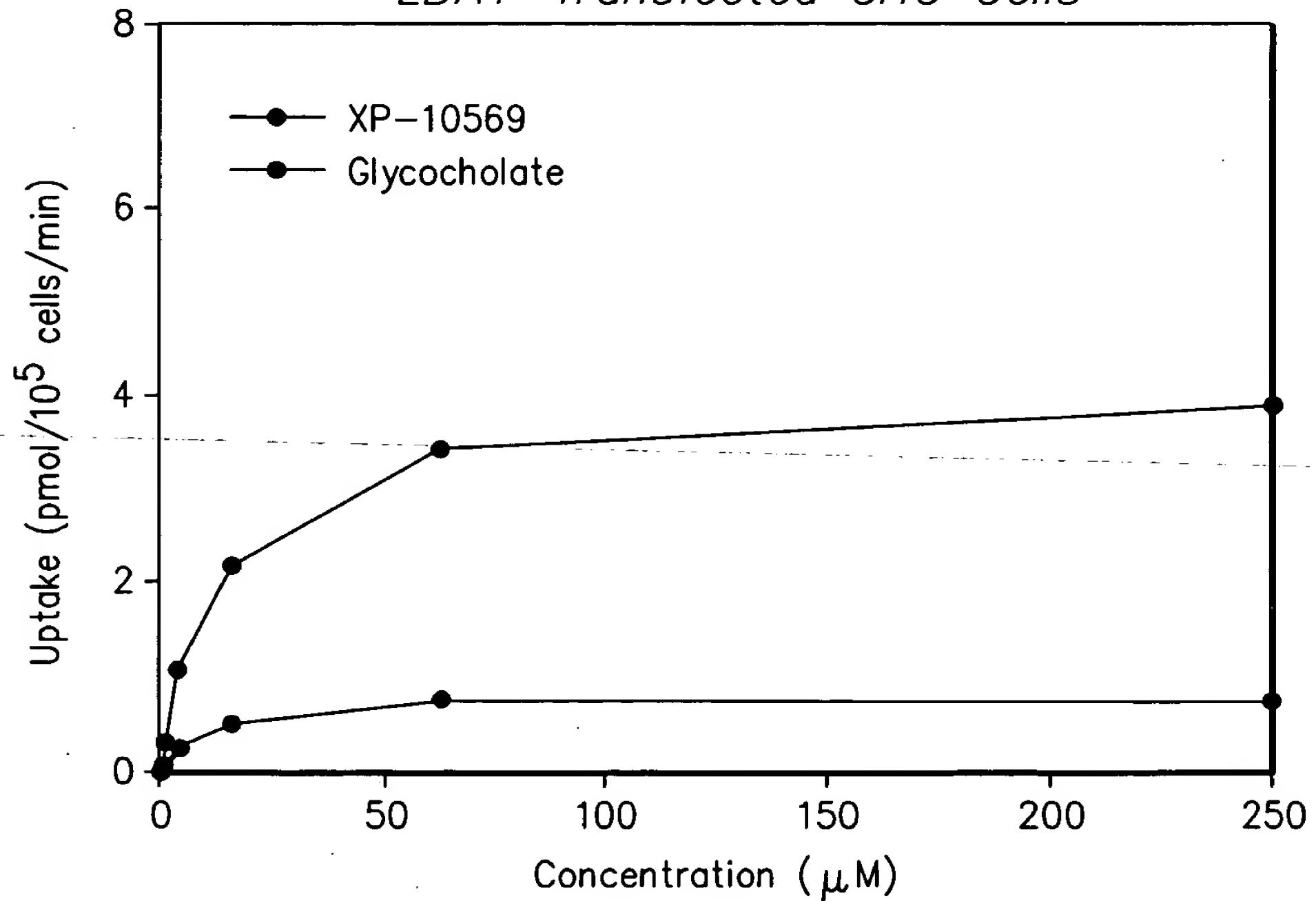
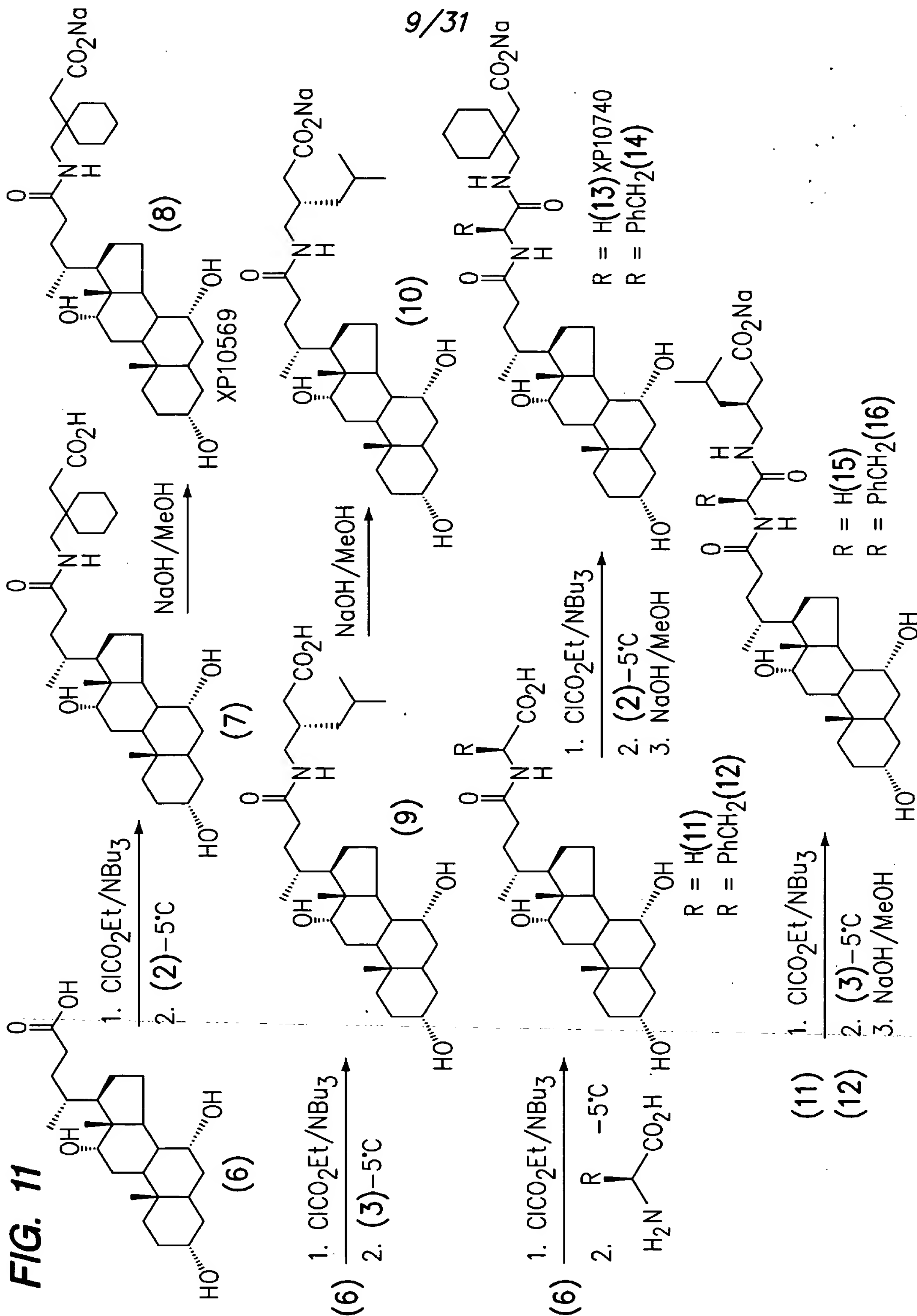
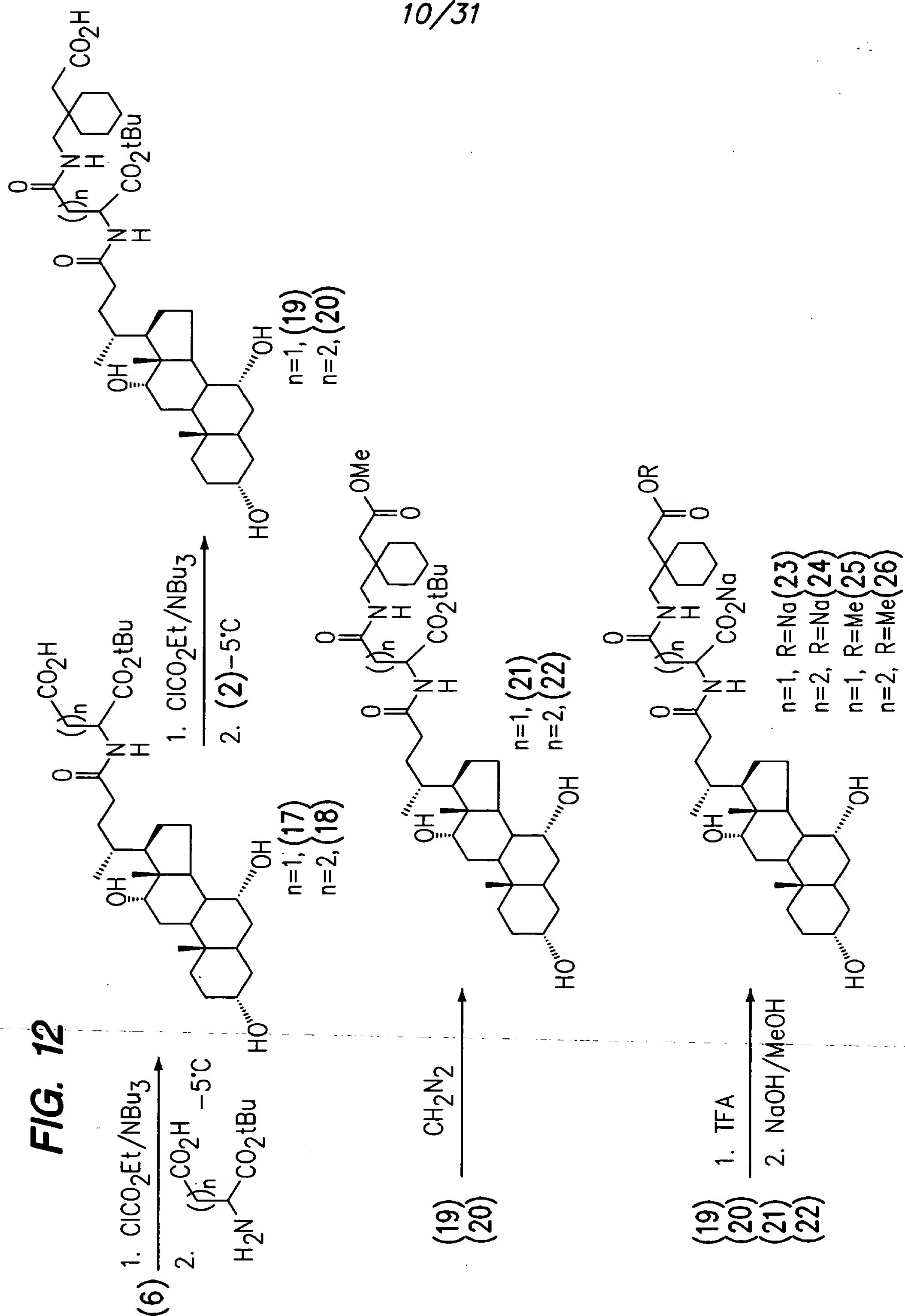




FIG. 11



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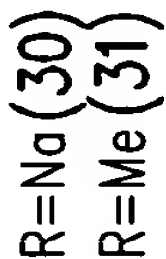
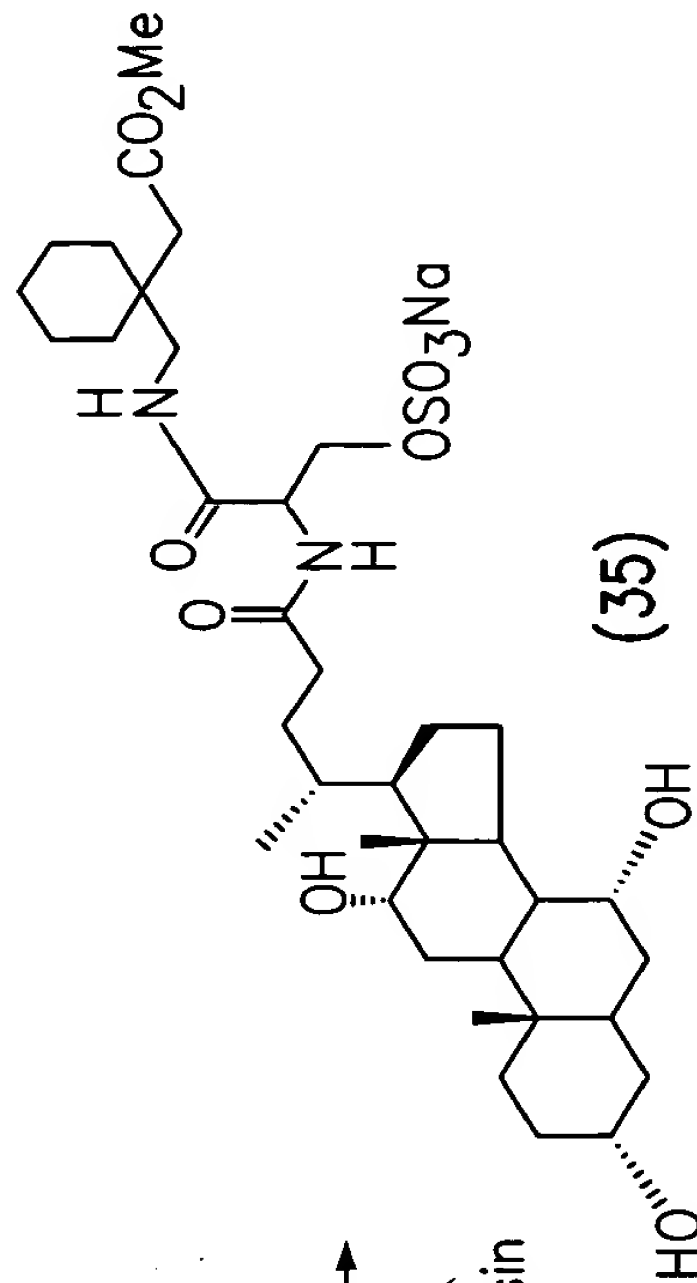
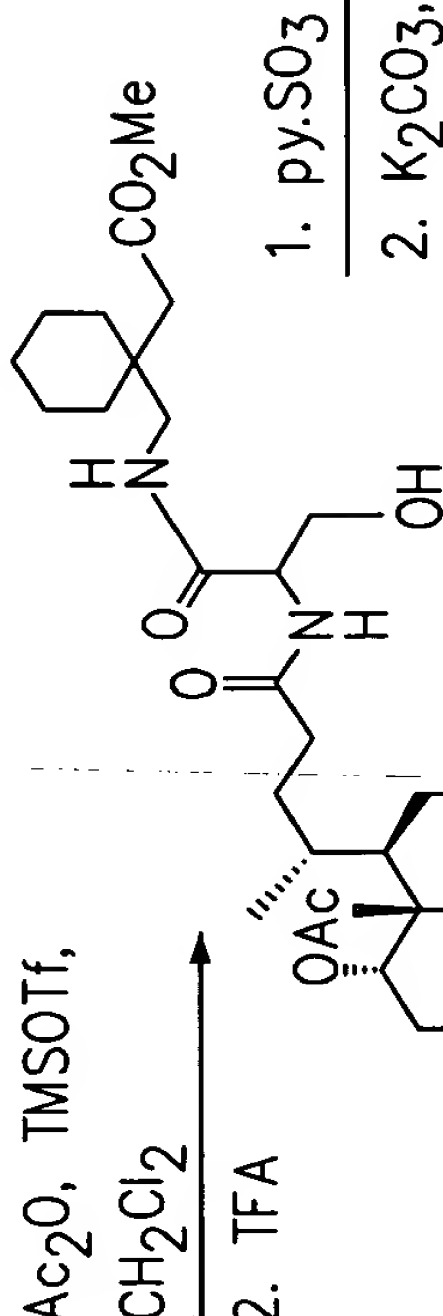
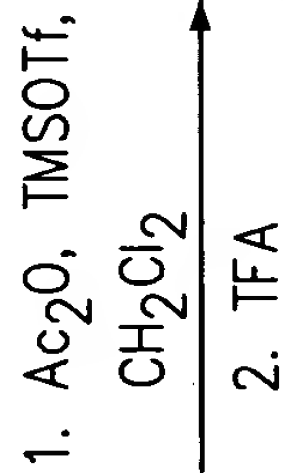
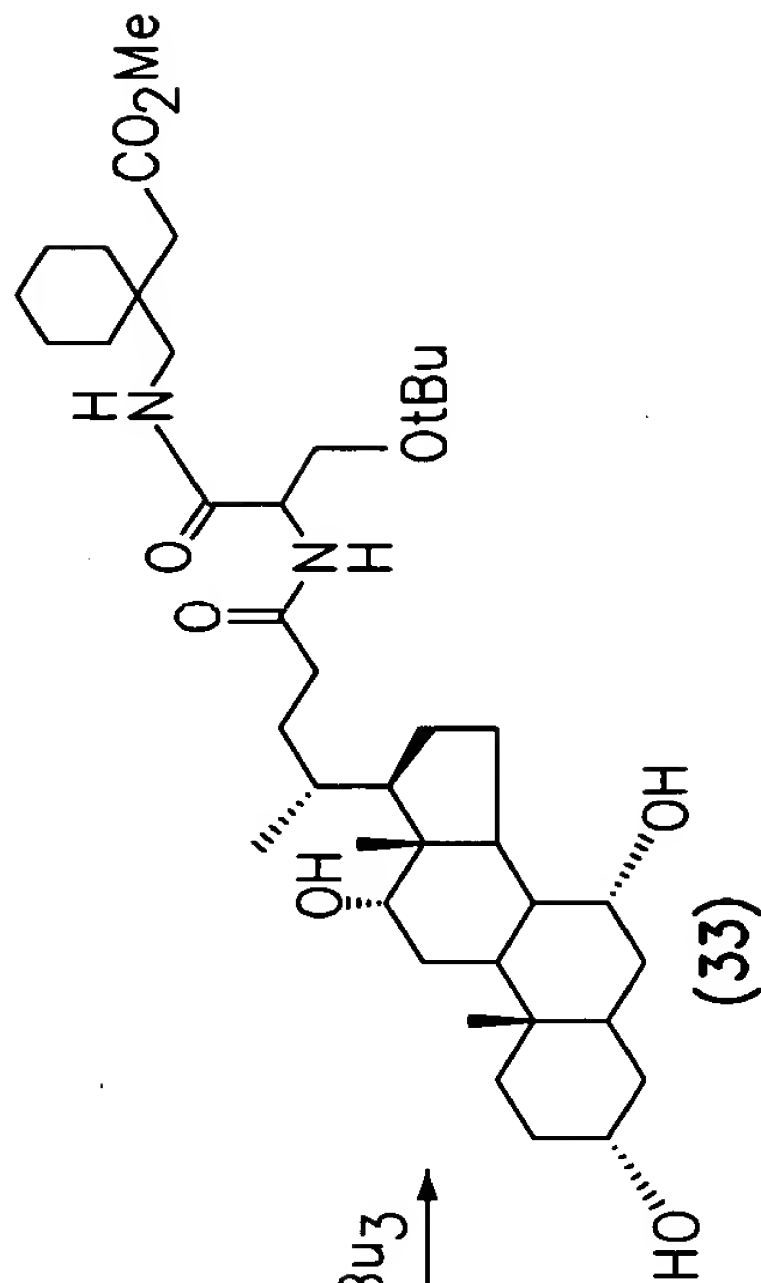
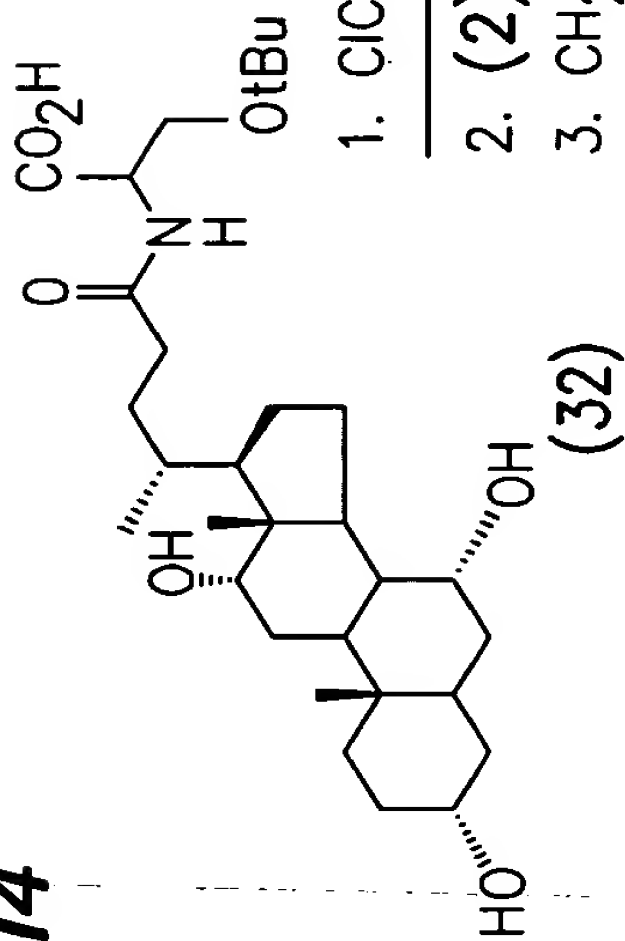
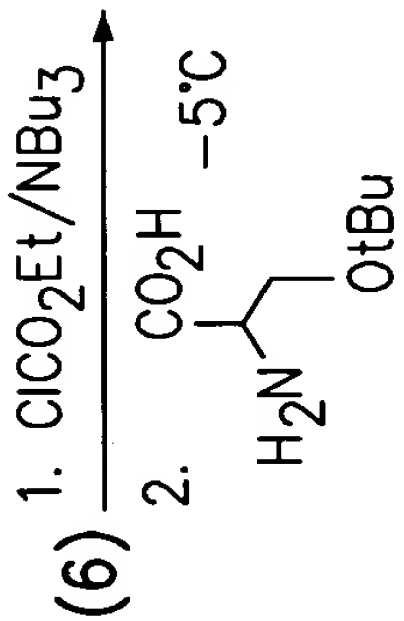
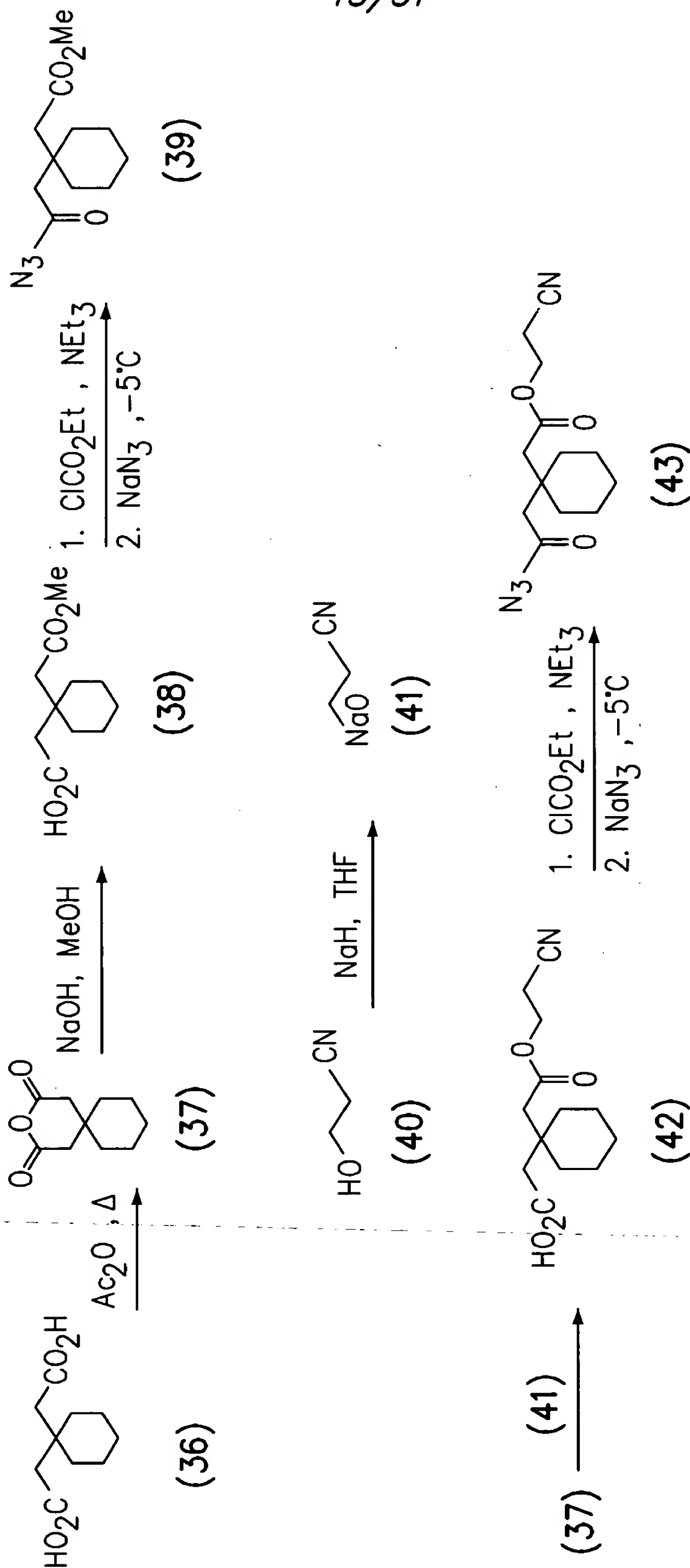


FIG. 14



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FIG. 15



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FIG. 16

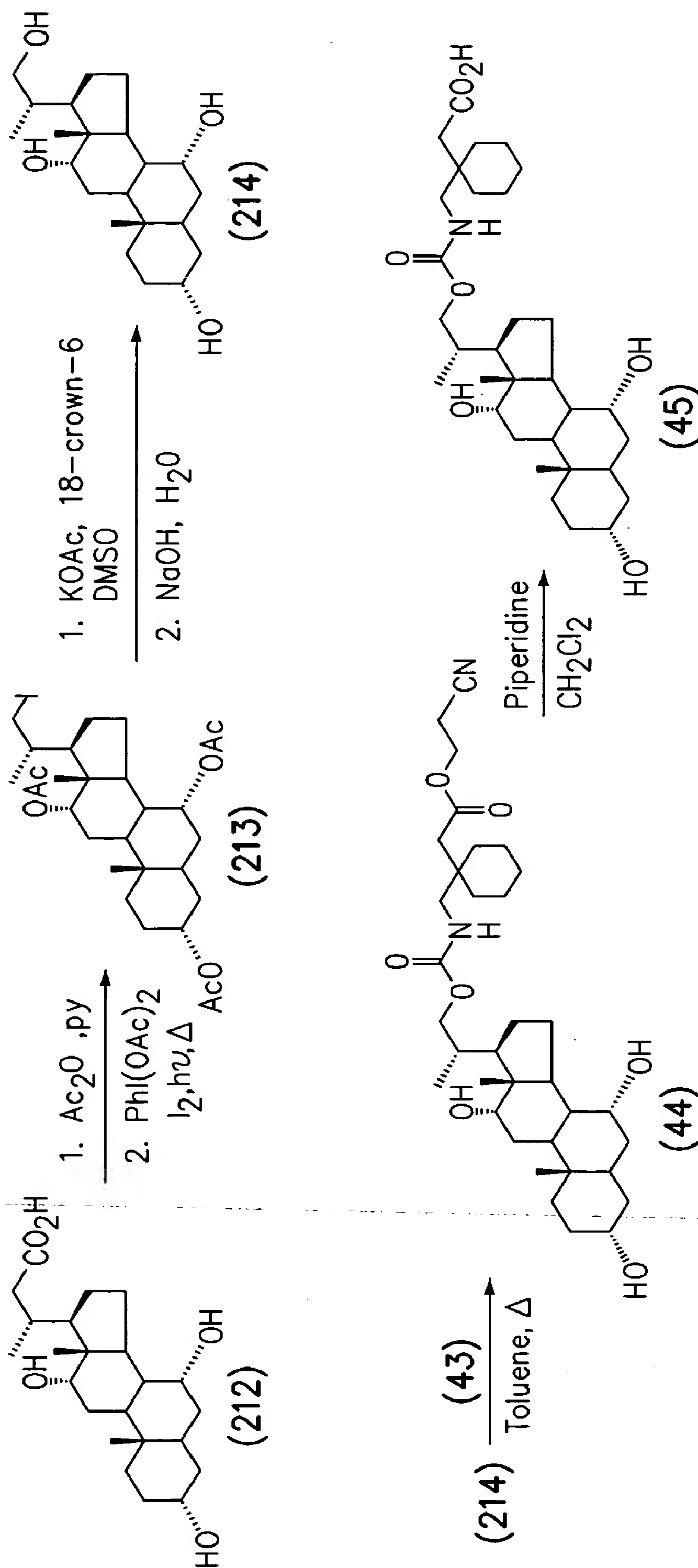


FIG. 17

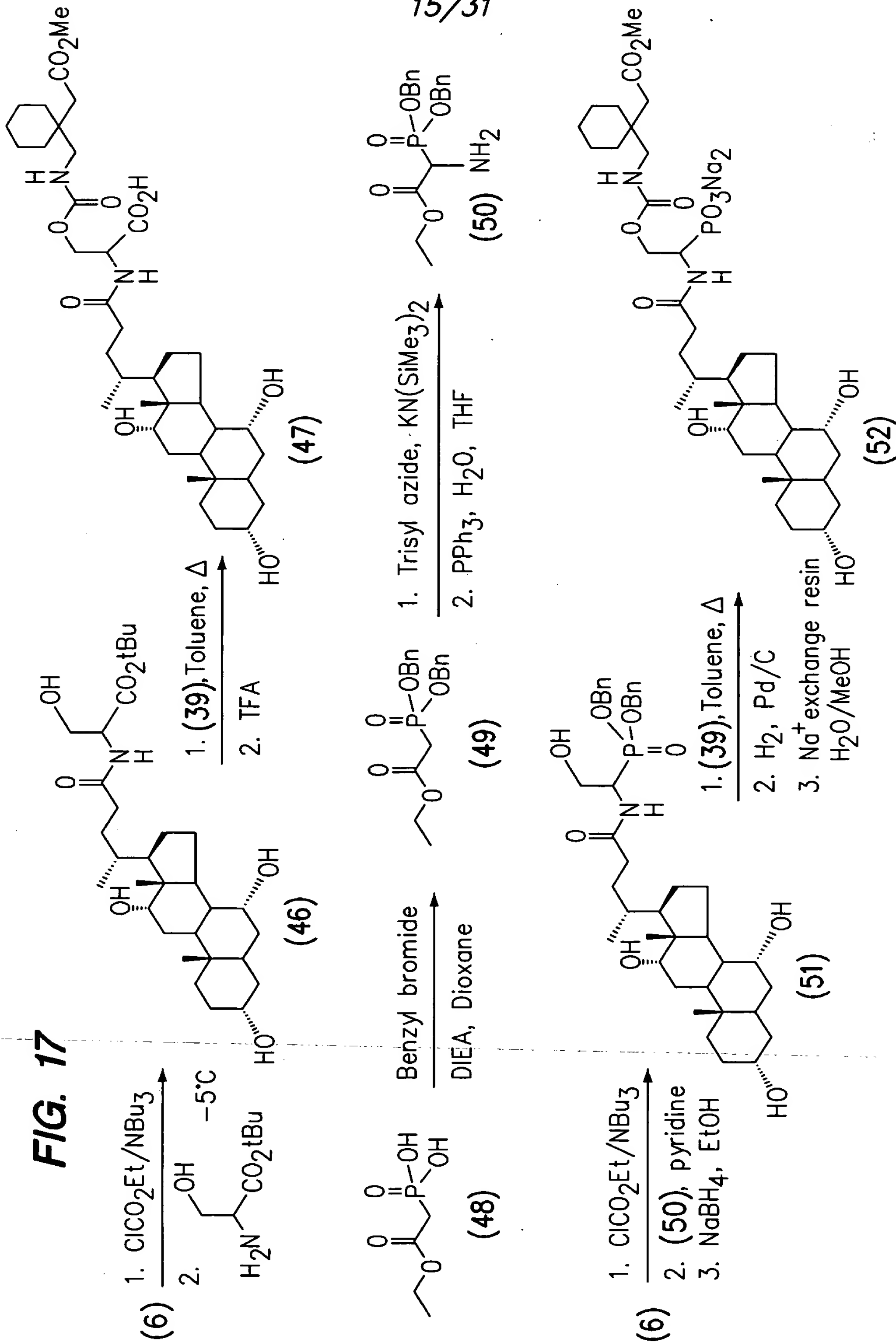
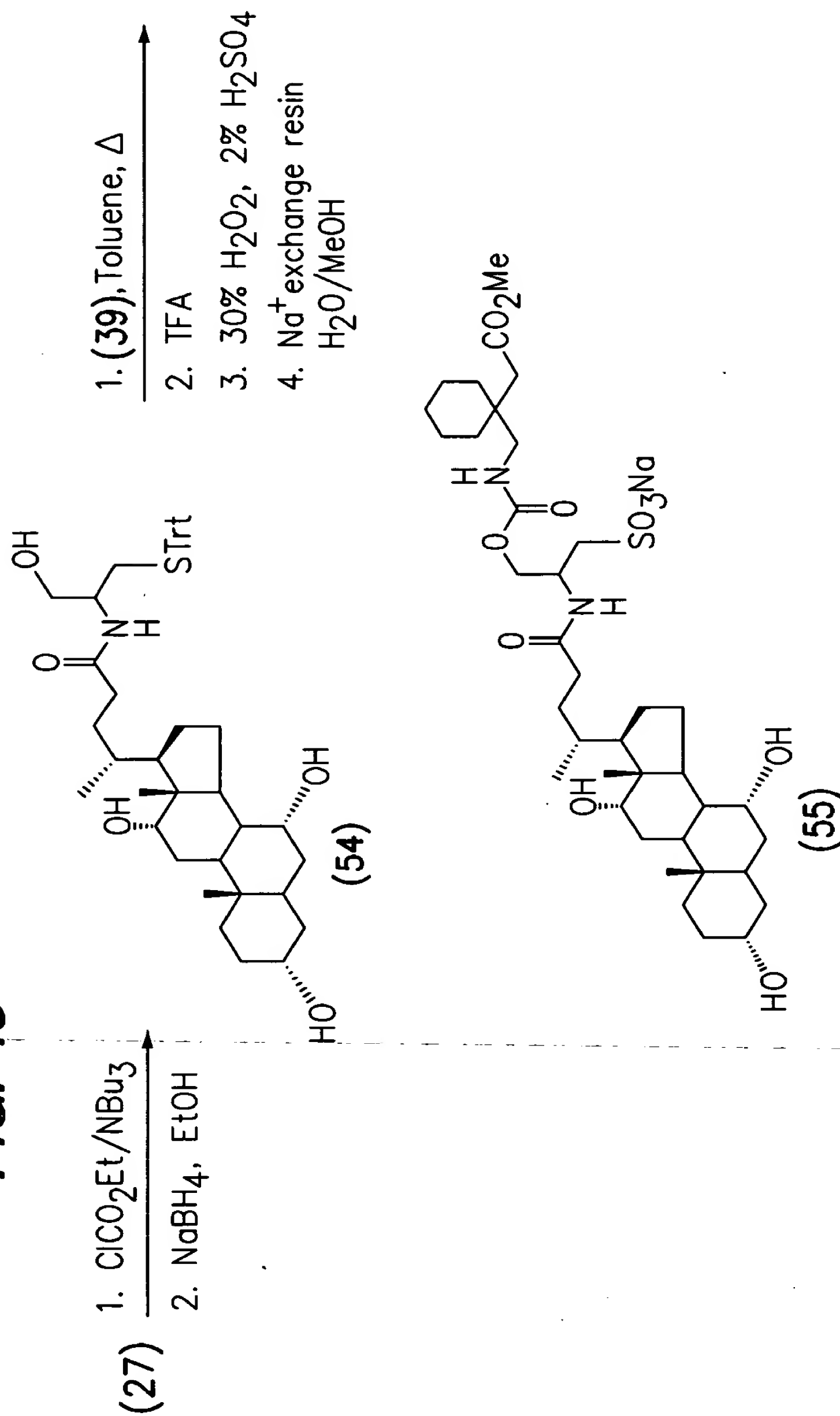


FIG. 18





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FIG. 19

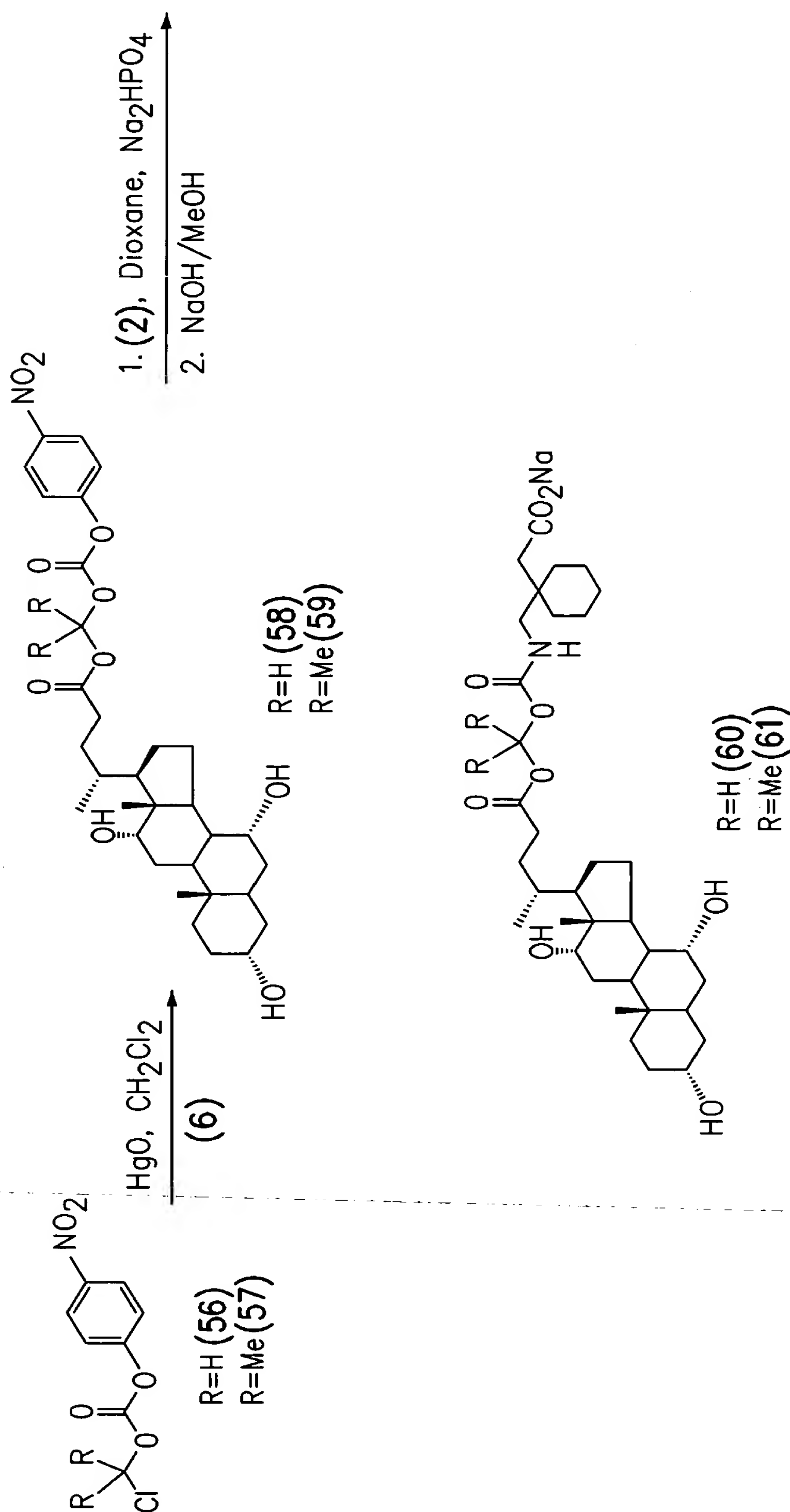


FIG. 20

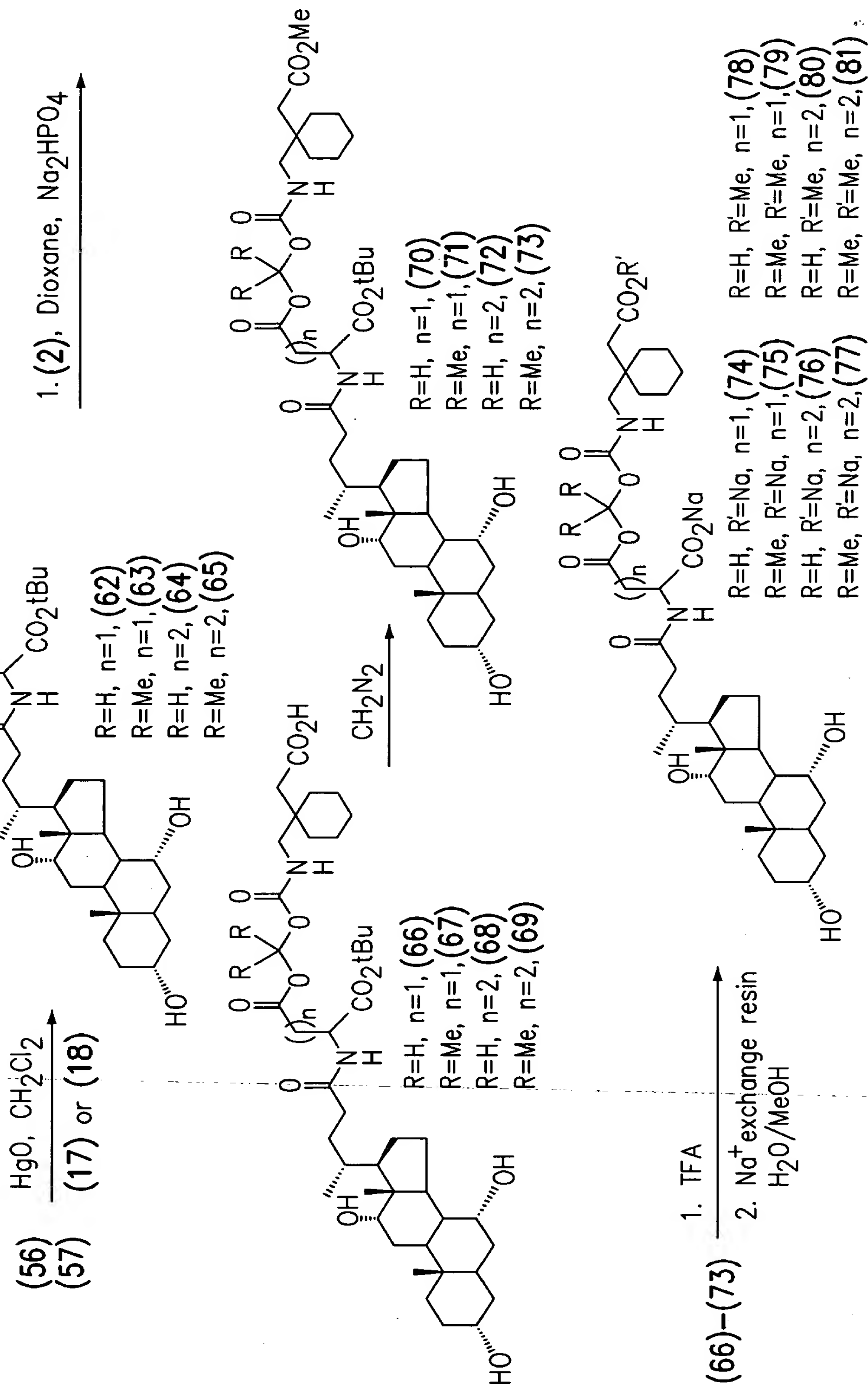


FIG. 21

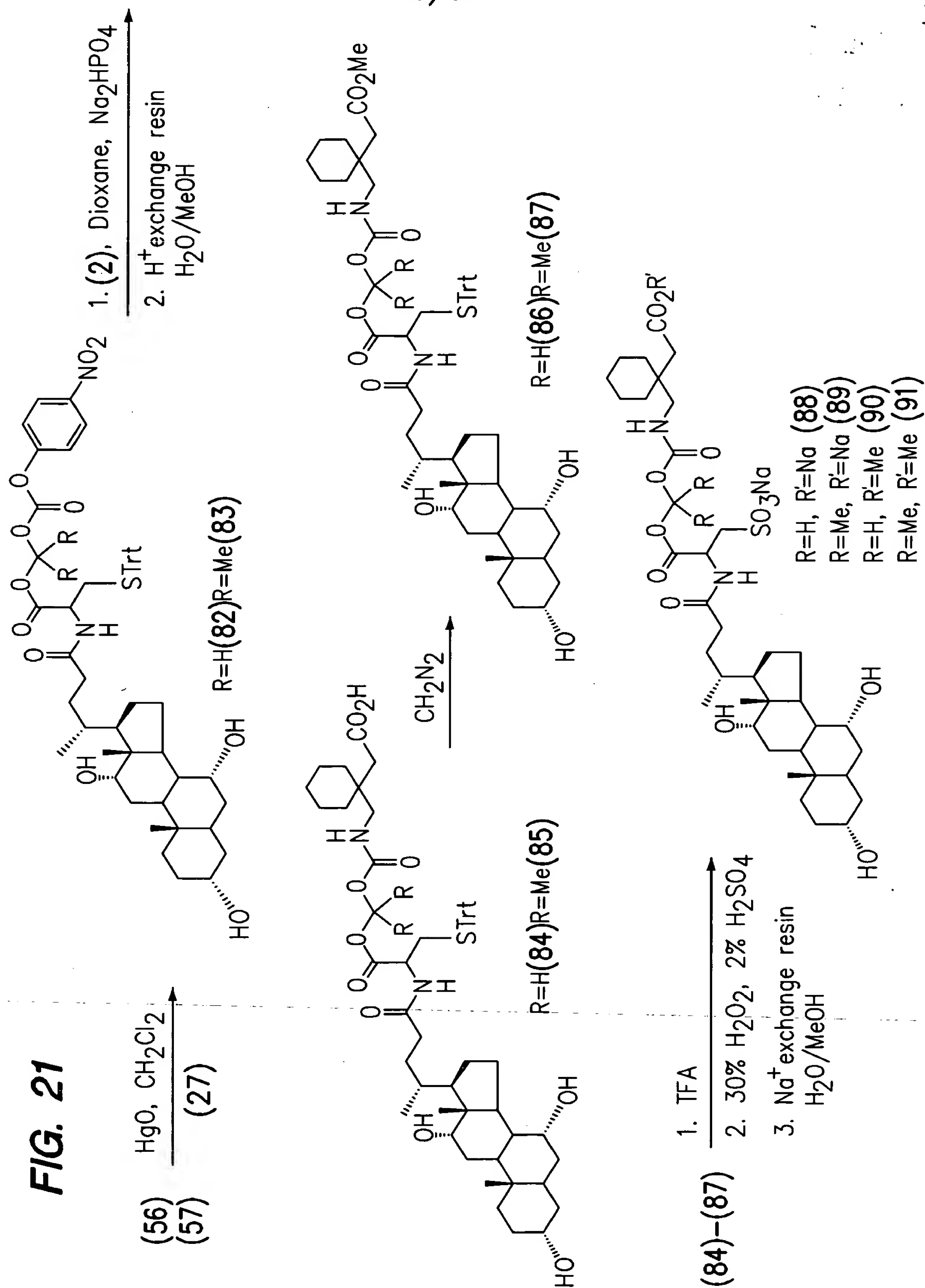
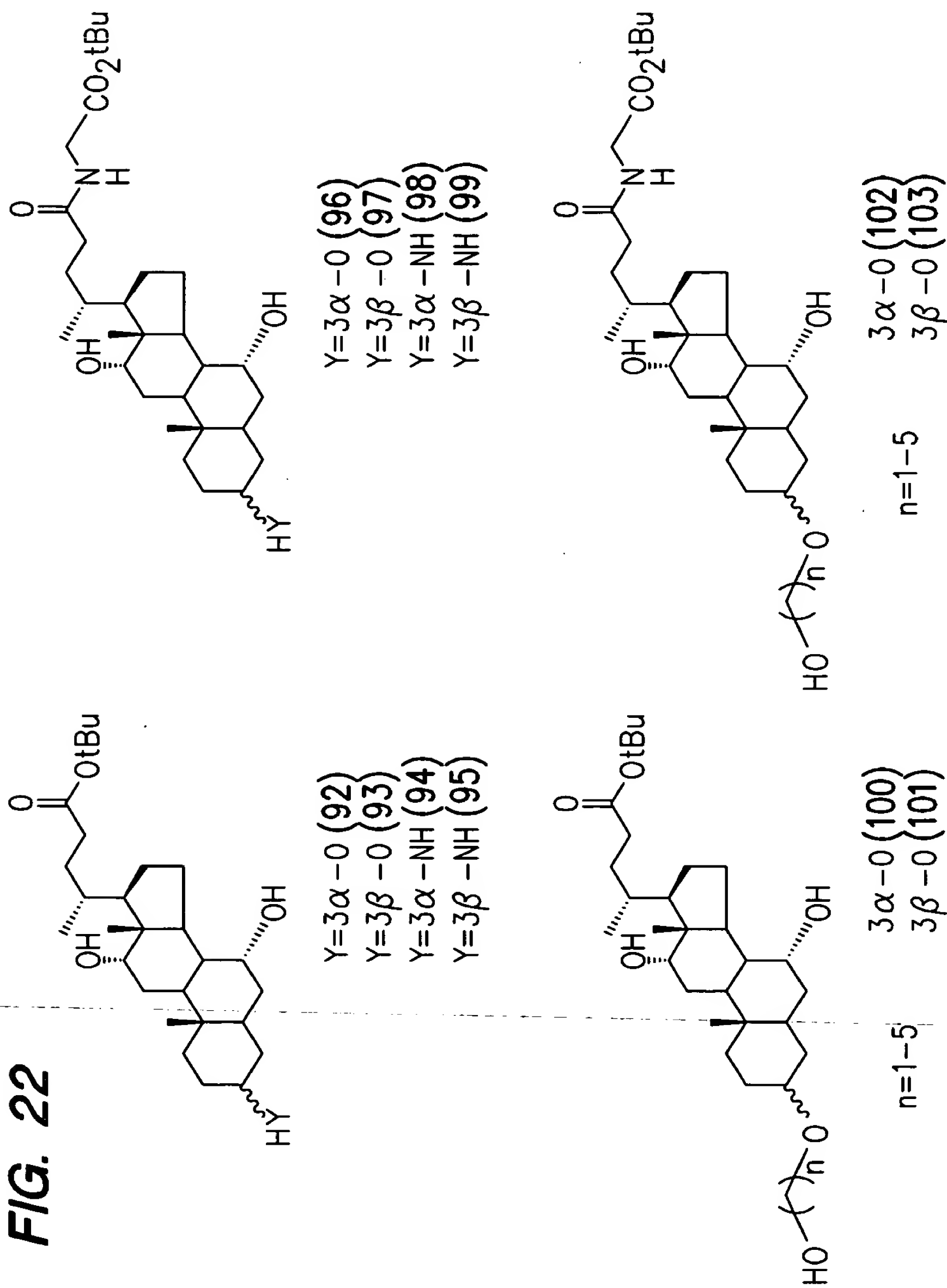


FIG. 22



Compounds (92)-(103) prepared following methods described in co-pending application "Bile Acid-Derived Compounds for Enhancing Oral Absorption and Systemic Bioavailability of Drugs" assigned to XenoPort, Inc.



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FIG. 24

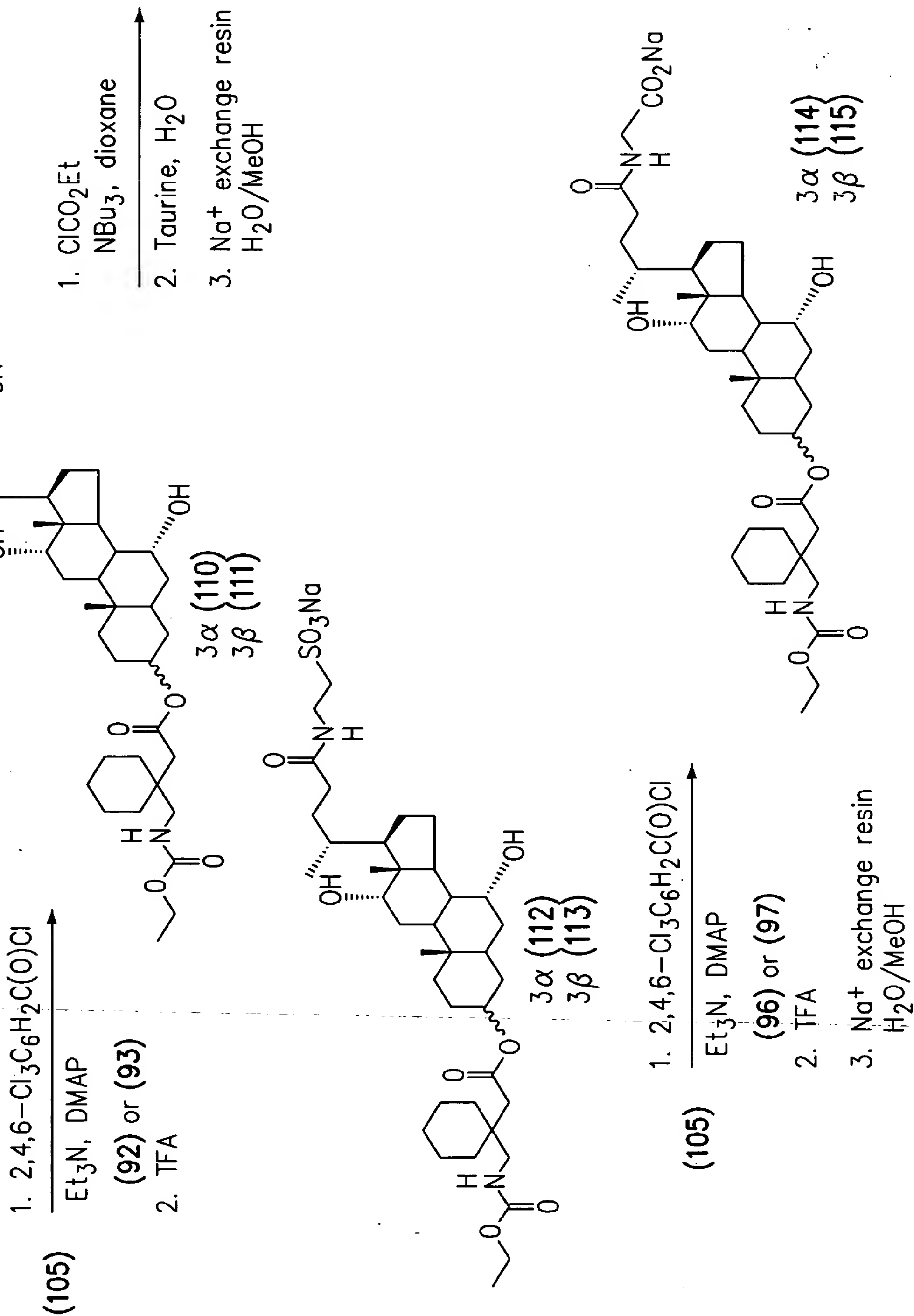


FIG. 25

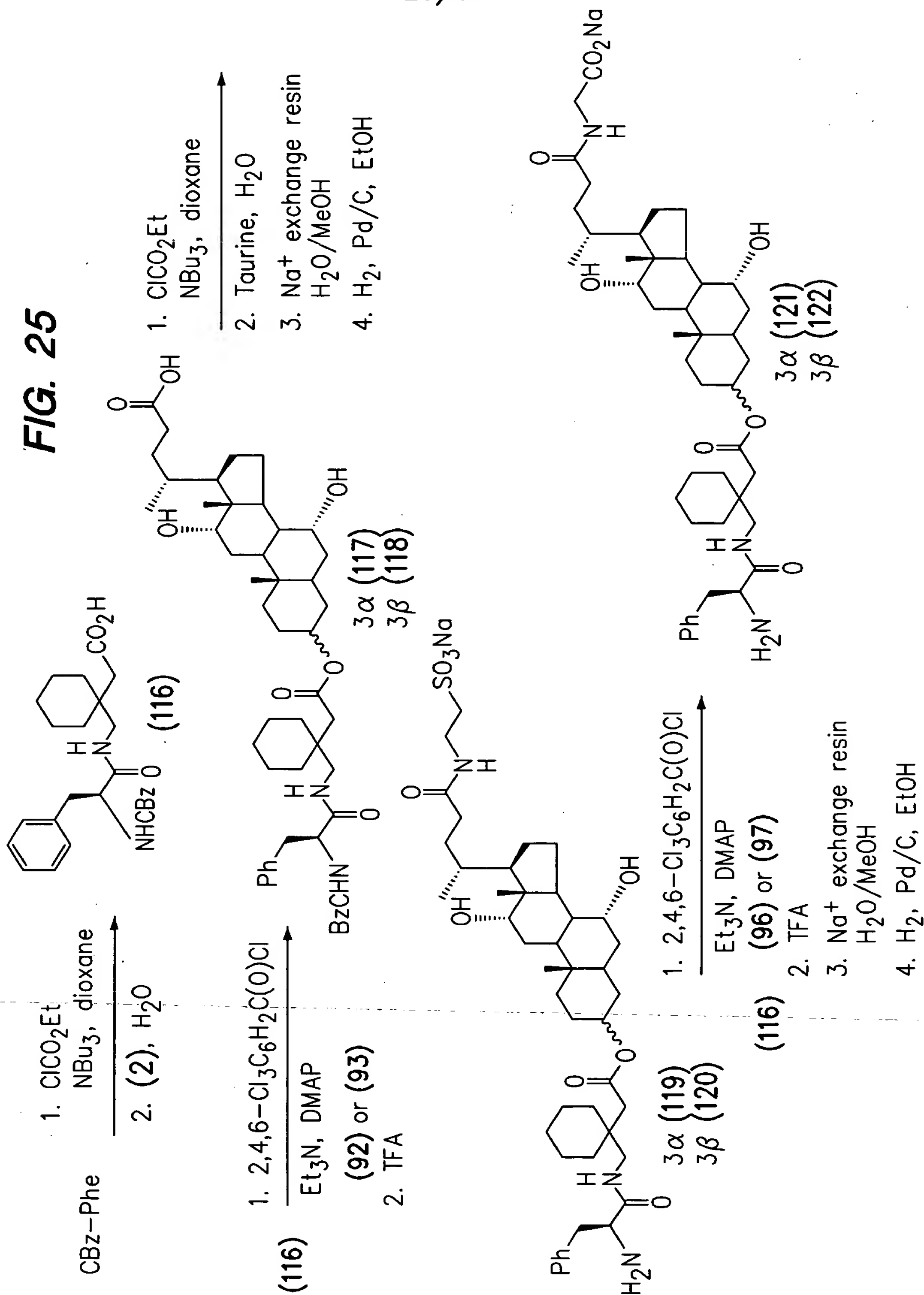
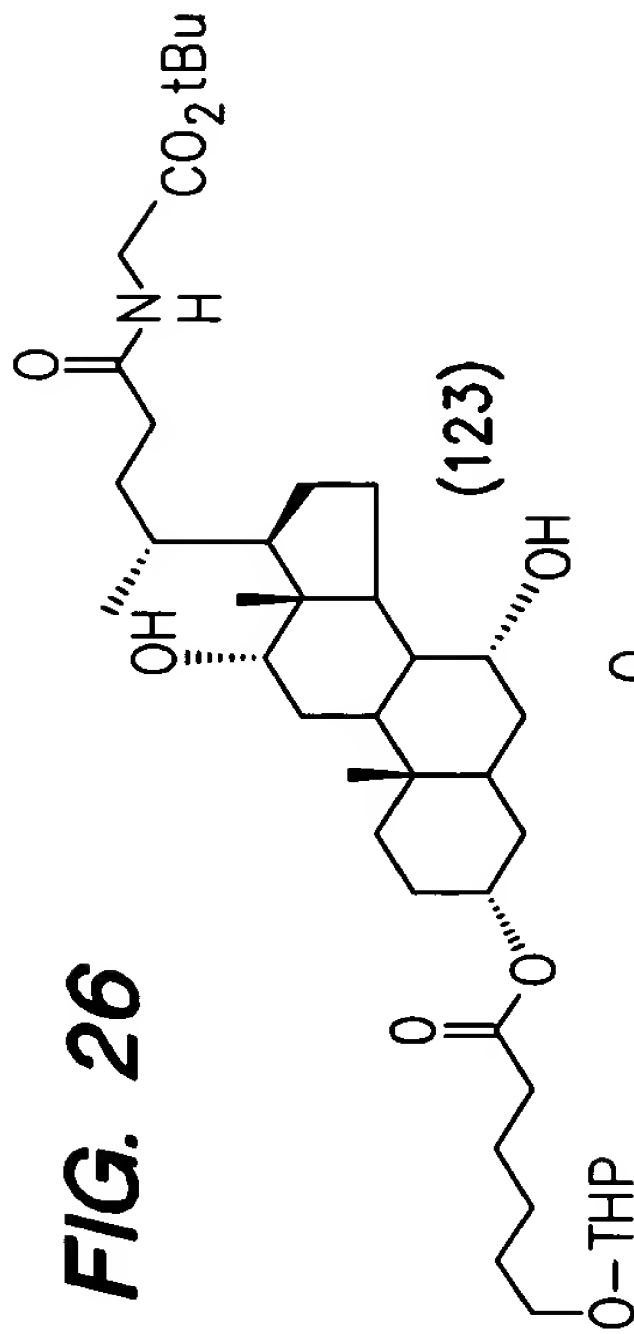
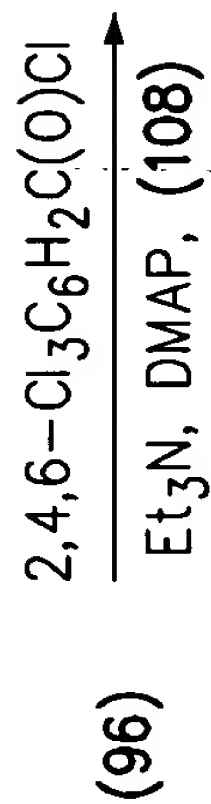
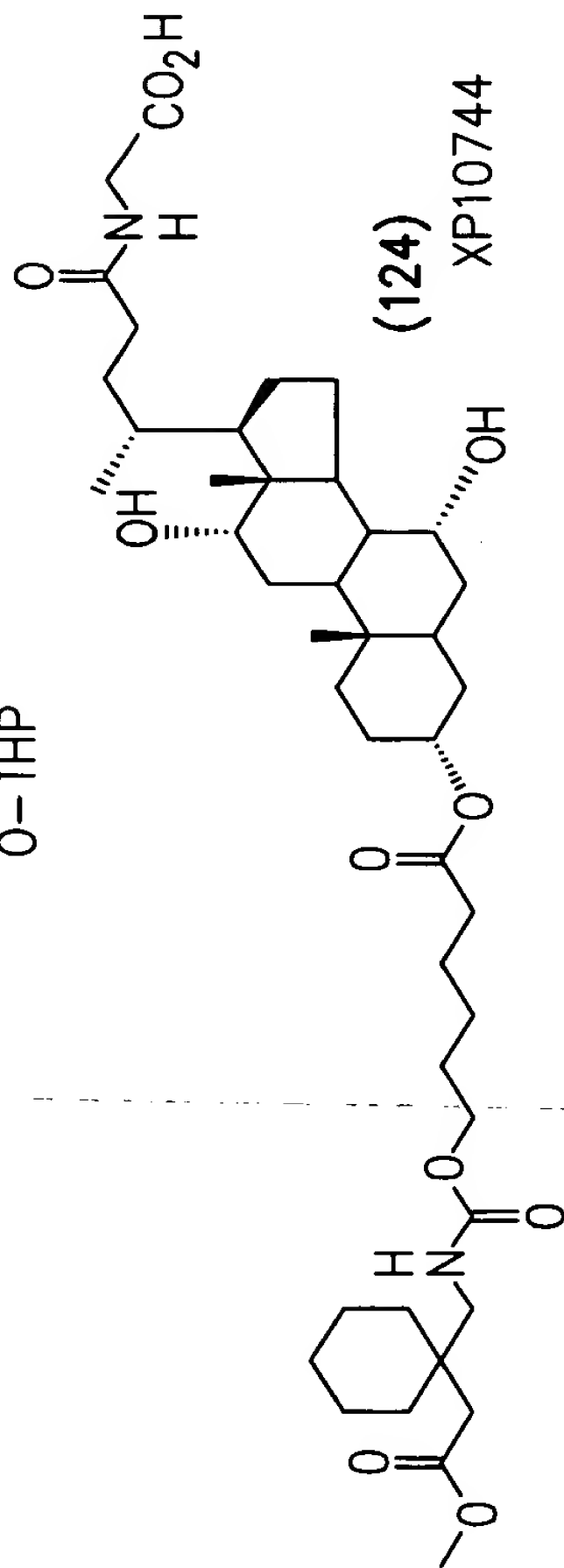


FIG. 26



1. PPTs, MeOH,  $\Delta$
2. (39), Toluene,  $\Delta$
3. TFA



- (109)  $\xrightarrow[\text{2. Piperidine, CH}_2\text{Cl}_2]{1. (39), \text{Toluene, } \Delta}$

1.  $\text{ClCO}_2\text{Et}$   
NBu<sub>3</sub>, dioxane
2. Taurine, H<sub>2</sub>O
3. Na<sup>+</sup> exchange resin  
H<sub>2</sub>O/MeOH

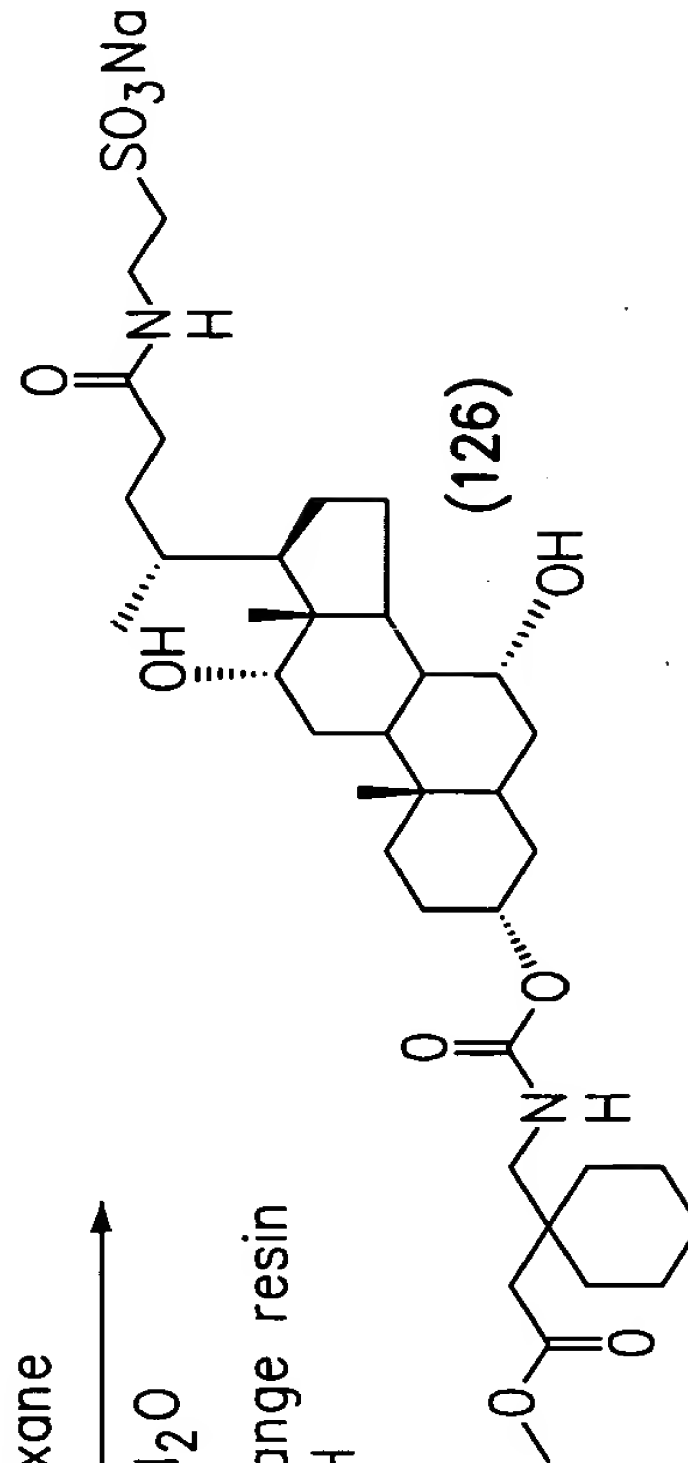
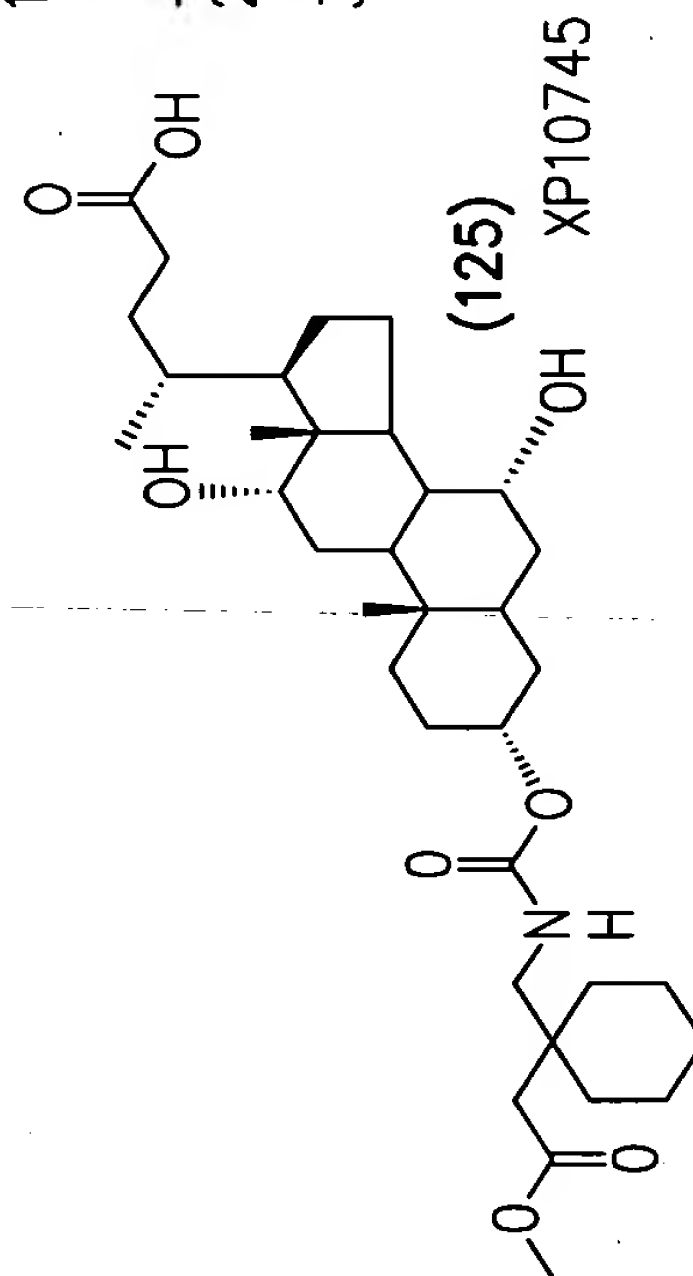
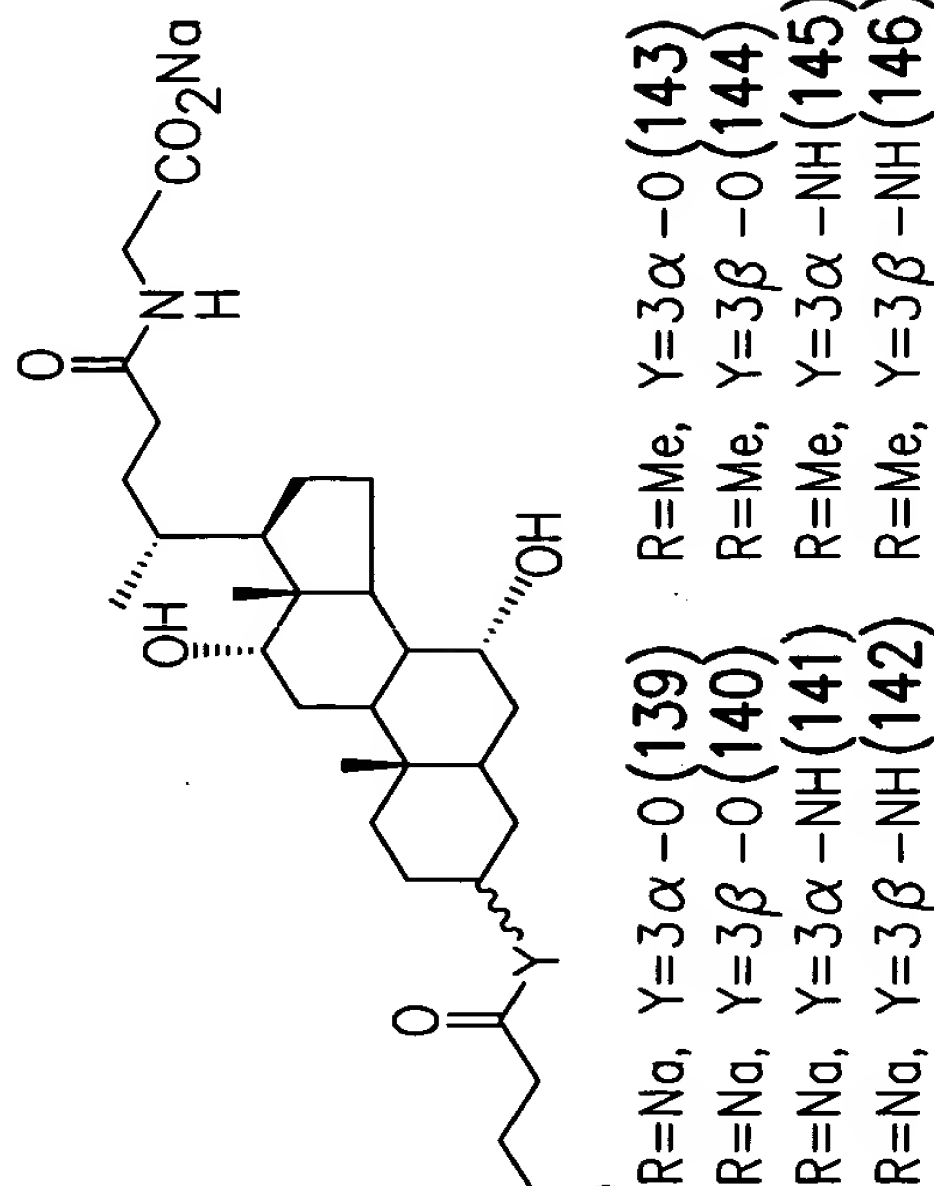
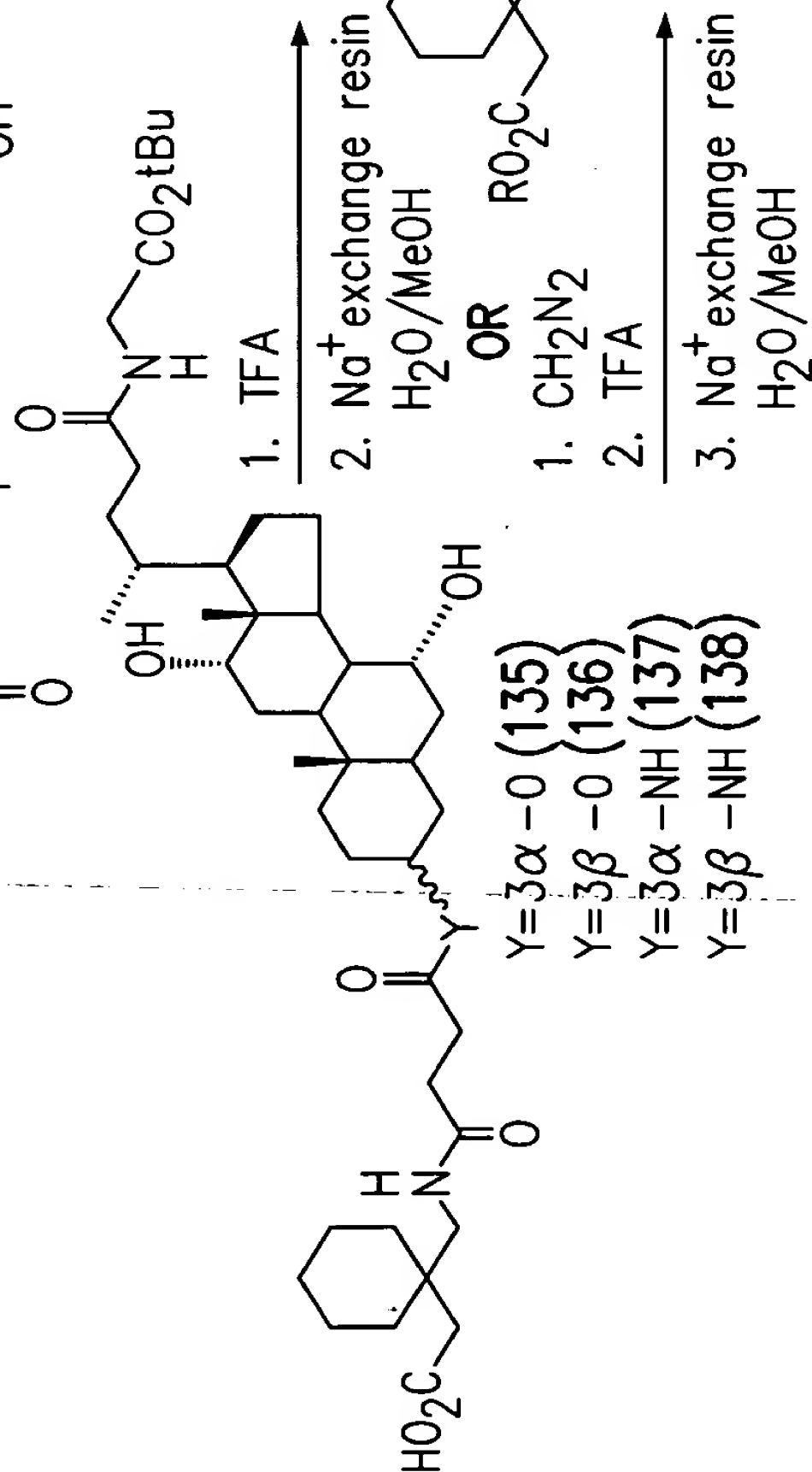
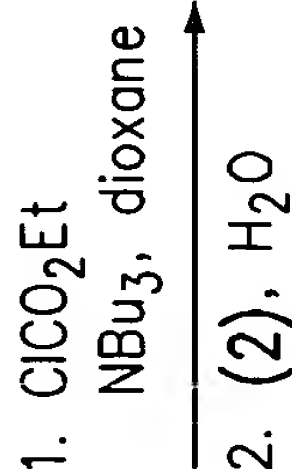
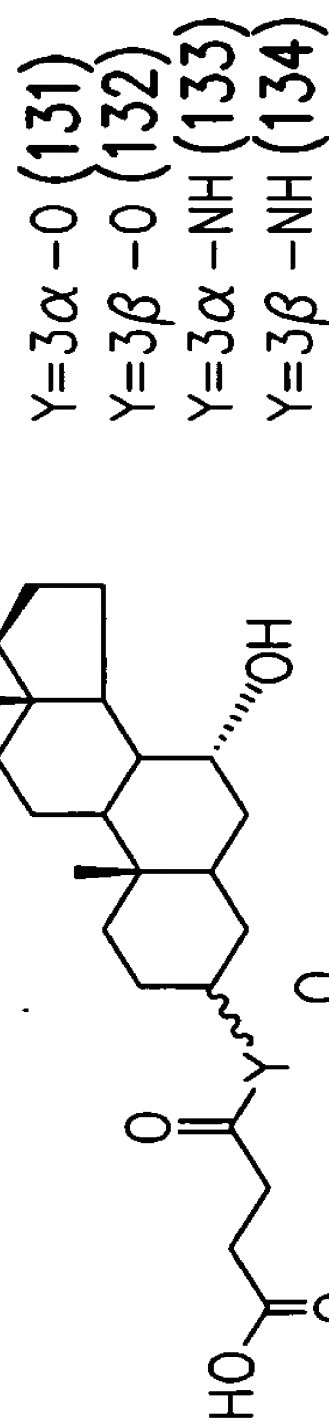
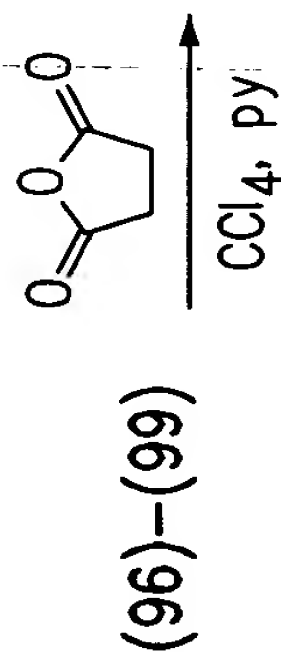
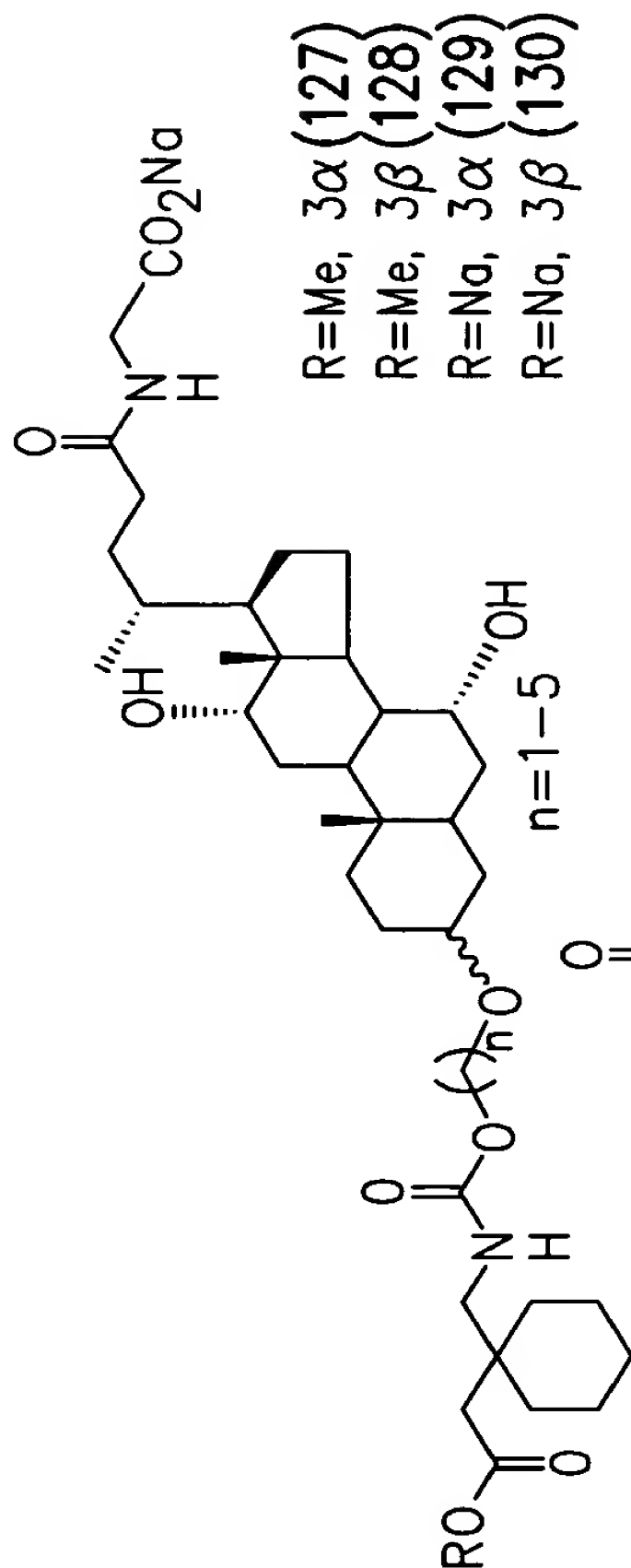
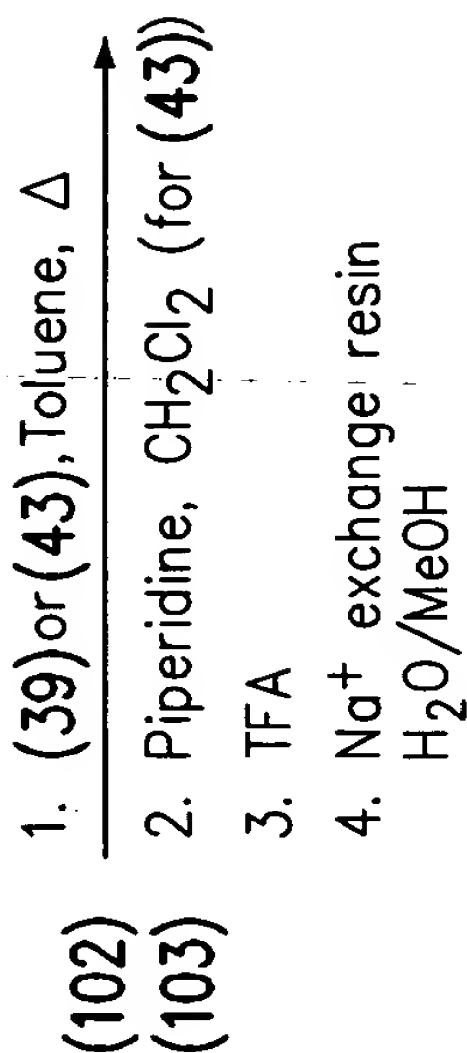
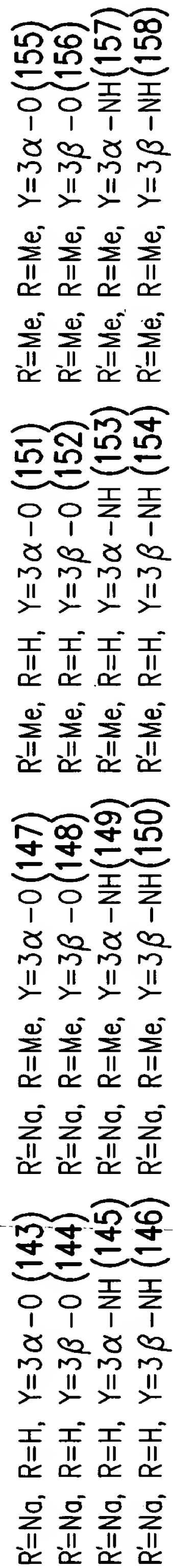
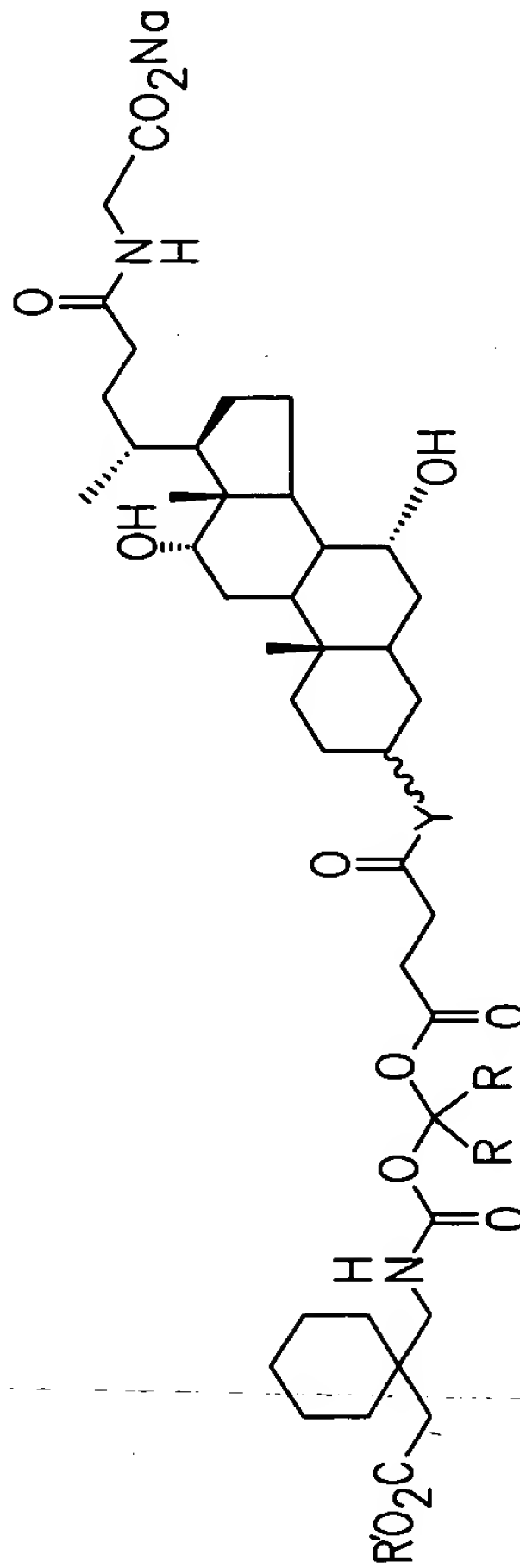
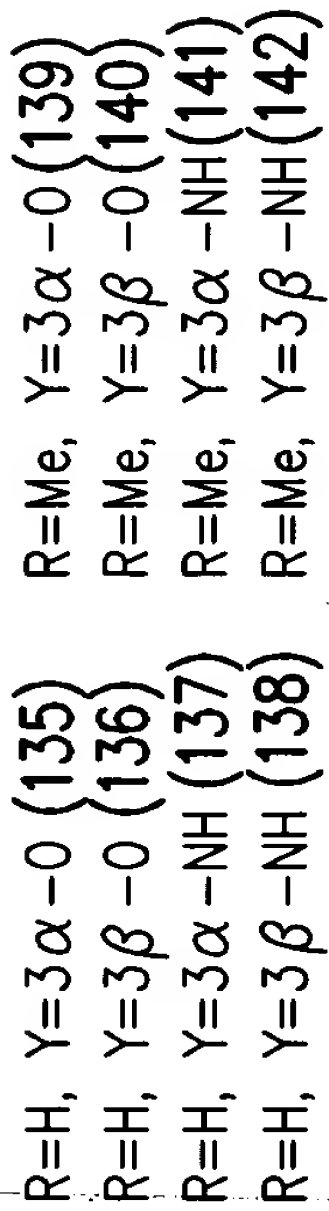
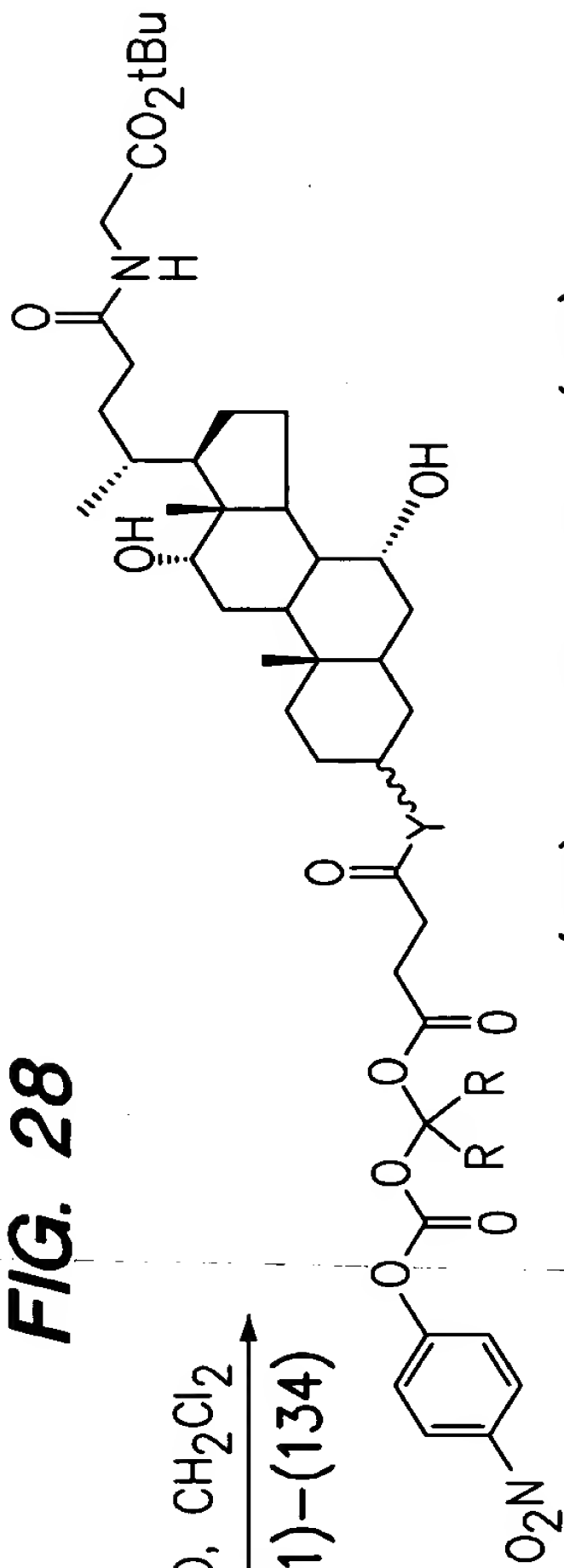
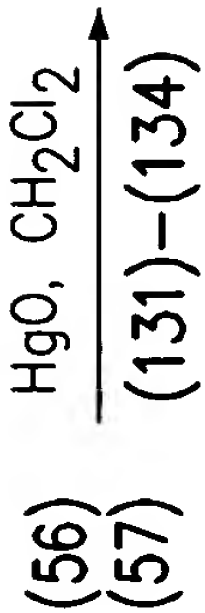




FIG. 27

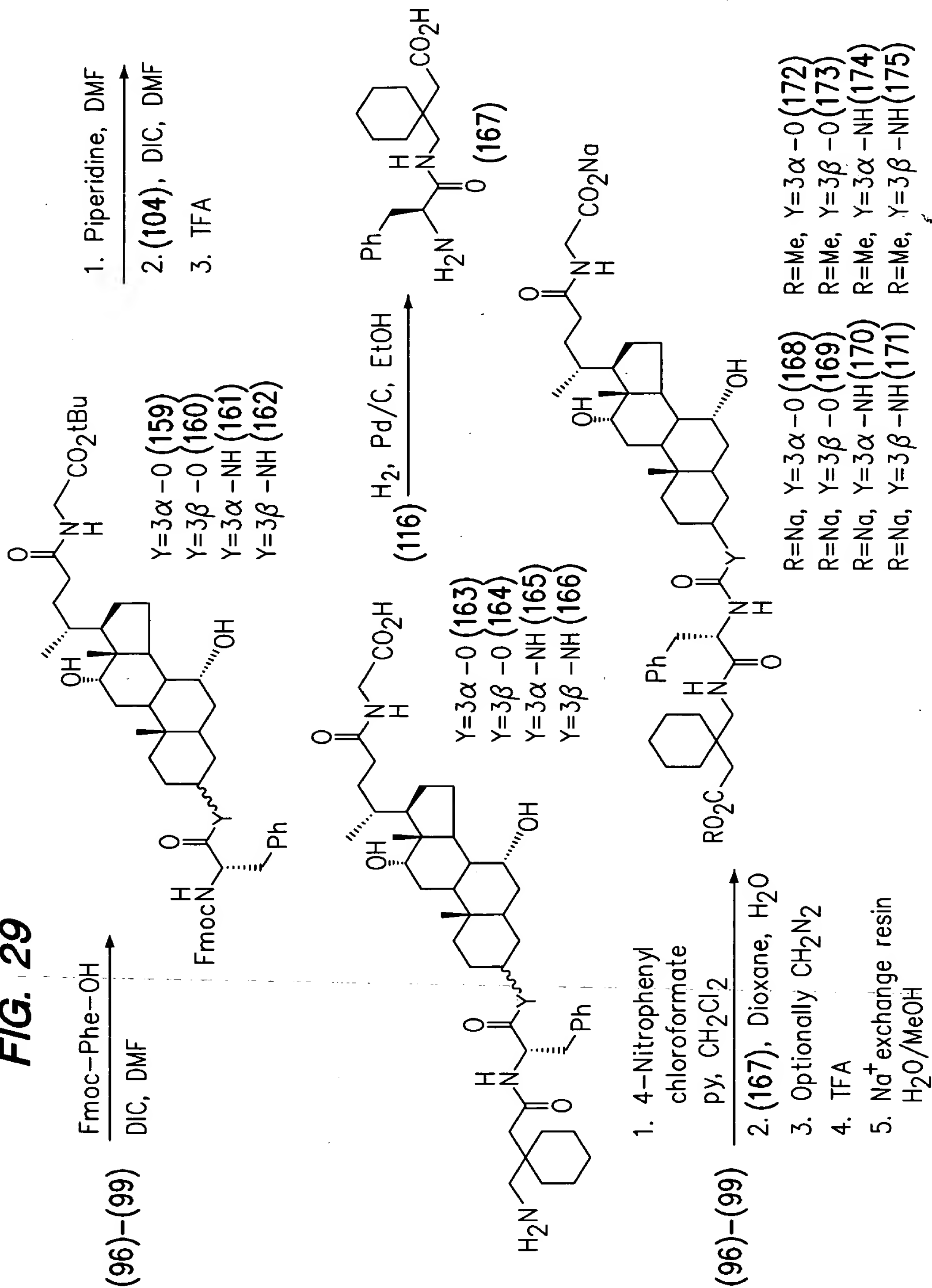


**FIG. 28**



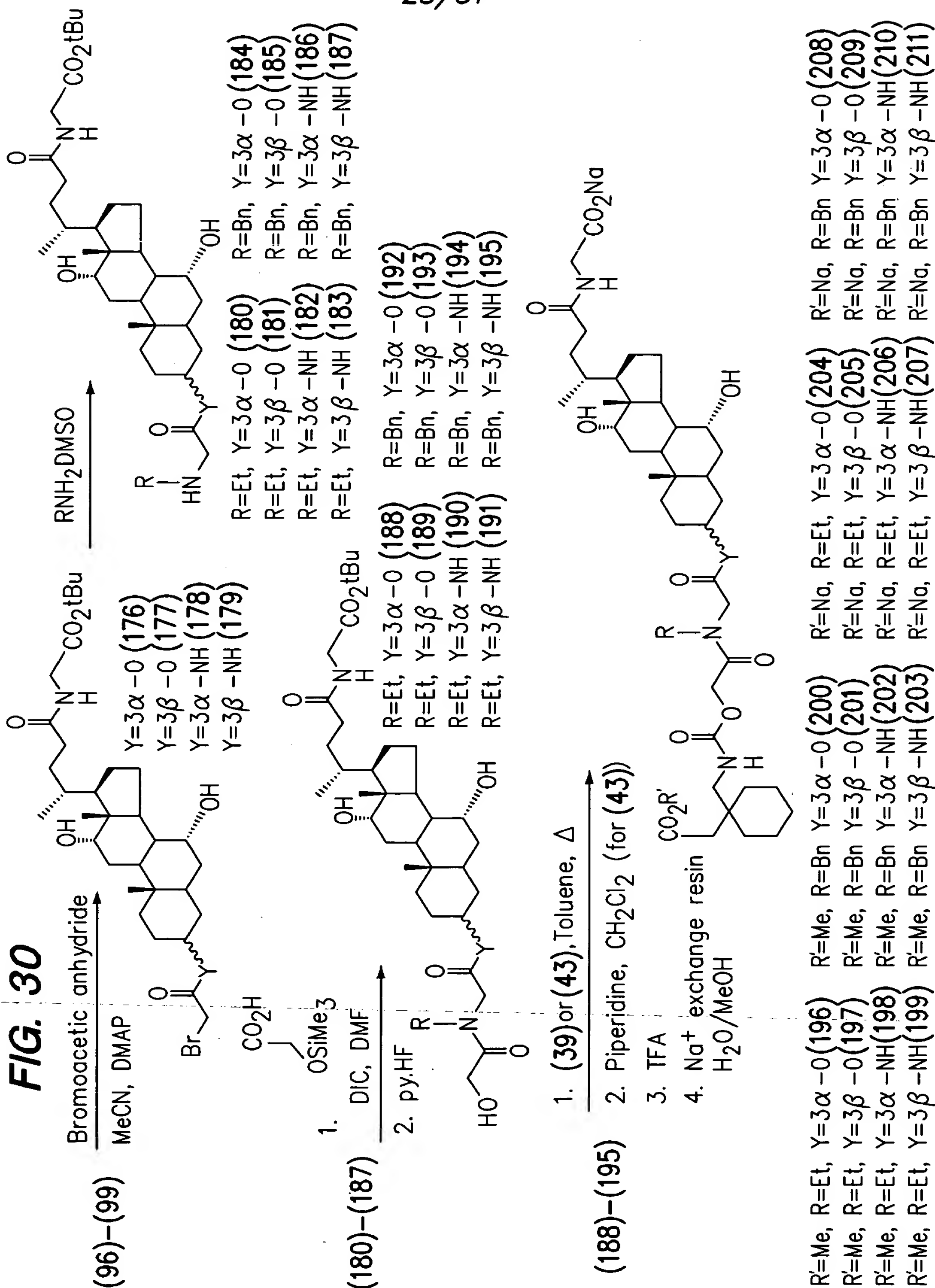
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FIG. 29



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FIG. 30



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FIG. 31

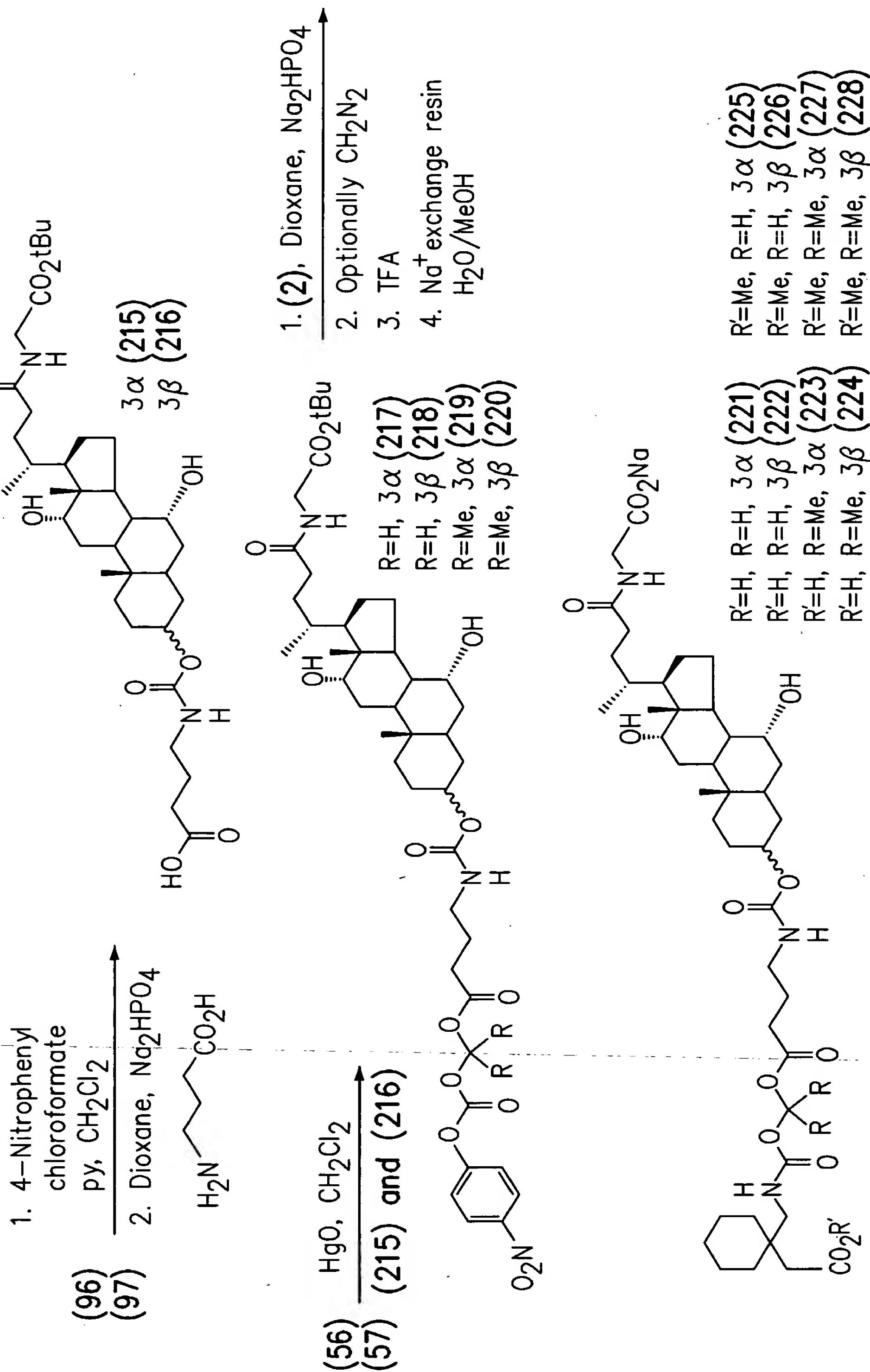
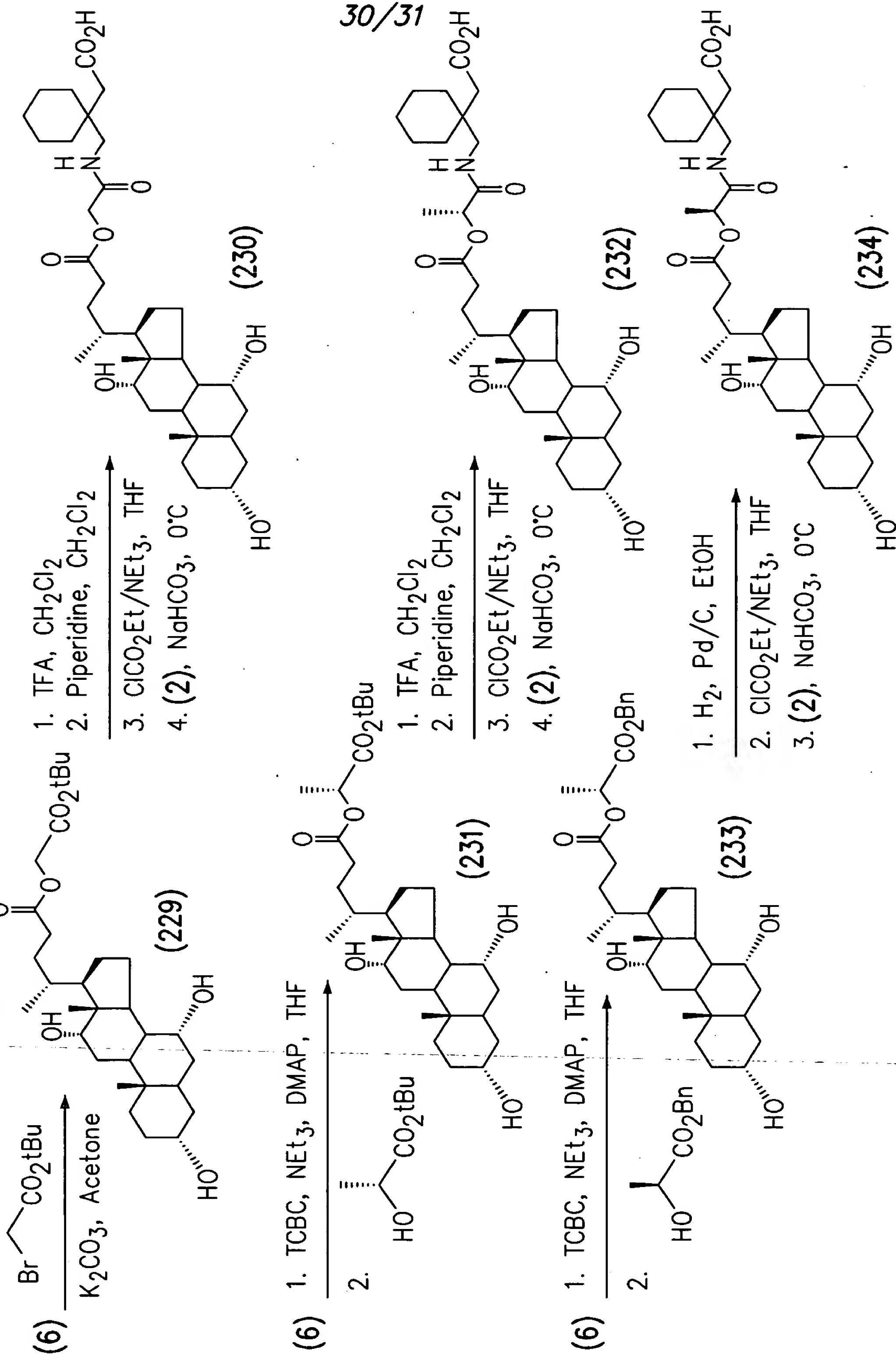


FIG. 32



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FIG. 33

